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THE RH BLOOD TYPES AND THEIR REACTIONS.

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LANDSTEINER AND WIENER (1940, 1941) described a new agglutinin which they found in the serum of rabbits immunized with the erythrocytes of the Rhesus monkey. The agglutinin reacted with the cells of about 85% of a sample of the white population of New York, independently of the blood groups or M,N types. The new property, which was designated "Rh" to indicate the manner in which it was discovered, would have aroused only passing interest had its discovery not been followed almost immediately by proof of its role in intragroup transfusion reactions (Wiener and Peters, 1940) and *erythroblastosis fœtalis* (hæmolytic disease of the newborn) (Levine *et alii*, 1941). Levine and Stetson (1939) had previously suggested that iso-immunization of the mother by foreign cellular antigen derived from the fœtus and inherited from the father was the cause of reactions following blood transfusions in a case they had investigated. Later, Levine (1942) showed statistically that the Rh factor was involved in about 90% of cases of hæmolytic disease of the newborn, and suggested that iso-immunization of the mother by fœtal antigen provided the key to the ætiology of this disease. The stimulus provided by these discoveries led to an intense study of the properties of the new factor resulting in a rapid accumulation of over 200 papers dealing with various aspects of its importance in clinical medicine, pathology, genetics and racial studies.

It was not long before it was discovered that various human anti-Rh sera did not give the same percentage of positive reactions (Levine *et alii*, 1941; Wiener, 1941). This proved that the Rh factor was not a single entity and led to the discovery of the various subtypes.

In England the importance of the Rh factor was quickly realized, and reports appeared in rapid succession confirming the part played by the Rh factor in the ætiology of hæmolytic disease of the newborn and in transfusion reactions. Almost simultaneously the story of the Rh subtypes was elucidated in the United States of America by Wiener and his associates, and by Race, Taylor and their associates in England, and it is from the many reports of these workers that our present knowledge of the Rh blood types has been obtained.

In our work in Australia we have to acknowledge that we have had the most generous cooperation and willingness to help with the supply of small quantities of the extremely rare Rh typing serum from Dr. A. S. Wiener, Dr. R. R. Race and the late Dr. G. L. Taylor.

Unfortunately the quantities of the subtype serum available have been necessarily small, so that we have been forced to restrict the number of blood samples tested for the Rh types in our racial studies in the south-west Pacific area.

The study of the Rh blood types was facilitated by the discovery by Levine and Javert (Levine, 1943) of a serum which reacted with all Rh-negative cells and certain Rh-positive cells. This serum was designated "Hr" to indicate its "reverse" relationship to the Rh factor. A similar but more potent serum was investigated by Race and Taylor (1943), and was named "St". Several other sera of the same specificity as the St serum have since been found.

INHERITANCE OF THE RH GENES.

The actual mechanism of inheritance of the various Rh genes has not yet been completely established. The six-gene theory of Wiener (1943) affords satisfactory explanation of the majority of cases, but occasional exceptions are found which can be explained only by the assumption that there are one or two additional genes.

The theory that is most commonly accepted now is that suggested by Fisher (Race, 1944), who postulated

the existence of eight allelic genes each associated with three antigens (or the existence of three loci so closely linked that they behave practically as a single entity). The three antigens associated with each gene may be any of six which react specifically with one only of six different kinds of serum (three kinds of Rh type serum and three of Hr type serum).

Fisher's theory predicted the existence of one new gene and two undiscovered Hr type sera, of which one has since been found. The Rhz gene (previously thought to be Rhy) has been identified by Murray, Race and Taylor (1945), and an additional Hr serum has been found and proved by Mourant (1945). The position is now that only one gene (Rhy), and one kind of anti-Hr serum, have yet to be discovered. The extra gene may have been encountered in our racial studies; but with the types of serum at present available we have no direct means of distinguishing between Fisher's Rhz and Rhy genes in the populations examined.

RH NOMENCLATURE.

With the rapid development of knowledge of the complex Rh factor simultaneously in different parts of the world, it was only natural that some confusion of terms and nomenclature should result. Several revisions of ideas have been necessitated by new discoveries; but it seems reasonable to suppose that Fisher's theory (which in any case may be easily extended should a new Rh type be identified) provides a fairly complete and practical description of the reactions of the various Rh blood types.

Several schemes have been suggested for the naming of the Rh genes and types, each of which has certain disadvantages. In an endeavour to achieve uniformity and if possible simplicity with regard to the Rh agglutinogens, and to provide guidance for the designation of any new blood factor that may be discovered, representative workers in various parts of the world have been asked to formulate rules for the naming of genes and to forward them, together with any other suggestions, to Dr. L. H. Snyder, of the United States of America, who has kindly undertaken to do the preparatory classifying prior to their consideration by an international committee.

In Table I are listed some of the suggested schemes for the nomenclature of the Rh genes and the reactions of these genes with the six specific sera.

Let us consider the advantages and disadvantages of each suggested nomenclature in turn.

1. Wiener's nomenclature has a right in priority. Its chief disadvantage is that it does not absolutely describe the reactions determined by the genes with the six types of antiserum. It is inconsistent in using both subscripts and superscripts, and, moreover, it is a little confusing in the use of Rh′ and Rh_1 for different genes. The terms "Rhy" and "Rhz" were first used by Race and his collaborators and have now been adopted by Wiener.[1]

2. Snyder's nomenclature is fairly simple and consistent in the use of superscripts only. It forecasts the reactions with the antisera for the six genes named. The only disadvantage is the retaining of the rather clumsy "prime" and "double prime" usage. Its main purpose, however, was to achieve uniformity in the use of superscripts only.

3. Race's (and Fisher's) nomenclature differs from Wiener's only in that "h" has been omitted from the "Rh". Wiener's nomenclature has been used in England to avoid confusion. The letters *C*, *D*, *E*, *c*, *d*, *e* and the Greek symbols Γ, Δ, H, γ, δ, η were not advanced as a suggested nomenclature, but were intended mainly to illustrate Fisher's theory, and in this respect they are of great value.

4. Murray's nomenclature is simple and systematic in respect of the genes, and it indicates the reactions to be expected with the six types of serum. It becomes unwieldy for phenotypes and is difficult to memorize.

5. The suggested nomenclature is simple, consistent and systematic. It indicates the reactions of the genes with the type antisera without ambiguity, and it is easily memorized. The "h" of the Rh has been dropped for simplicity in naming the genes and to provide a means of differentiating between genes and phenotypes. It is considered desirable to retain the "Rh" in full for the phenotypes to conform to usage; but there is no clinical danger in departing from the earliest designation for the Rh genes.

Extension of Suggested Nomenclature Number 5.

The reversed letters "Rh" and "Hr" might well be retained for the antisera to indicate the reverse manner in which these sera react. For example, anti-Rh^1 serum reacts only with genes the designations of which include the superscript "1"; anti-Hr^1 serum reacts only with those genes the designations of which do not include the superscript "1".

The Rh Genes.

Perusal of Table I will show that the reactions of each of the genes with all six types of serum may be obtained without ambiguity from their designation.

The genes react only with the anti-Rh sera referred to in their superscripts. With the anti-Hr sera they react

[1] Throughout this paper we have referred to "the reactions of genes", in lieu of the more precise term "reactions of the antigens determined by the genes". It should be noted also, that the "Rh genes" are probably a combination of three or more closely linked genes.

TABLE I.

The Rh Genes and their Reactions with Antisera.

Nomenclature of Genes According to					Reactions with Antisera.						Author.
					Δ	Γ	H	δ	γ	η	Fisher.[5]
					D	C	E	d	c	e	Race.[3]
					3	1	2	6	4	5	Murray.[4]
					Anti-Rh_0	Anti-Rh′	Anti-Rh″	Anti-Hr_0	Anti-Hr′	Anti-Hr″	Wiener.[1]
Wiener[1]	Snyder[2]	Race *et alii*[3] and Fisher[5]		Murray[4]	Graydon and Simmons	Anti-Rh^0	Anti-Rh^1	Anti-Rh^2	Anti-Hr^0	Anti-Hr^1	Anti-Hr^2	Graydon and Simmons.
rh	rh	R	cde	Rh456	r (or R)	−	−	−	+	+	+	
Rh_0	Rh^0	R″	cDe	Rh345	R^0	+	−	−	−	+	+	
Rh′	Rh′	R′	Cde	Rh156	R^1	−	+	−	+	−	+	
Rh″	Rh″	R′	cdE	Rh246	R^2	−	−	+	+	+	−	
Rh_1	$Rh^{0'}$	R_1	CDe	Rh135	R^{01} (Orally, R "oh one")	+	+	−	−	−	+	
Rh_2	$Rh^{0''}$	R_2	cDE	Rh234	R^{02}	+	−	+	−	+	−	
Rhy		Ry	CdE	Rh126	R^{12}	−	+	+	+	−	−	
Rhz		Rz	CDE	Rh123	R^{012}	+	+	+	−	−	−	

The Rhy gene and the anti-Hr^0 serum have yet to be discovered.

[1] A. S. Wiener, 1945.
[2] L. H. Snyder, 1945.
[3] R. R. Race, G. L. Taylor, E. W. Ikin and A. M. Prior, 1944.
[4] J. Murray, 1944.
[5] R. R. Race, 1944.
[6] Alongside the symbols used by Race *et alii*, we have listed their analytical equivalents in terms of the elementary antigens designated by those authors as *D*, *C*, *E*, *d*, *c*, *e* reacting with the antisera Rh^0, Rh^1, Rh^2, Hr^0, Hr^1 and Hr^2 respectively

only with those not mentioned in the superscripts. For example, gene R^{02} (pronounced R "oh two") reacts with anti-Rh^0 serum and anti-Rh^2 serum, but not with anti-Rh^1 serum. Gene R^{02} reacts with anti-Hr^1 serum, but not with anti-Hr^0 or anti-Hr^2 serum. Thus the designation R^{02} determines the reactions of the gene so called with each of the six types of serum. This notation automatically indicates the composition of each gene in terms of the hypothetical elementary antigens required by Fisher's theory. For example, gene R^{02} might be written $R^{02}H^1$ and the genotype $R^{01}r$ (Fisher's *CDe/cde*) might readily be expanded to R^{01} H^2/H^{012}.

The Rh Phenotypes.

Now let us see how this terminology may be applied to the Rh phenotypes, the "h's" being retained to distinguish the phenotypes from the genes. In Table II the proposed scheme is compared with Wiener's, which has been used in the majority of the published papers dealing with the Rh blood types. Wiener's nomenclature does not indicate fully the reactions of the phenotypes with anti-Rh type sera or with the anti-Hr type sera. The proposed designations are completely descriptive of the reactions of the cells in respect of the anti-Rh sera, but are not adequate with regard to the reactions with the anti-Hr sera. With one exception, all the phenotypes include at least two types of cells which give different reactions with one or more of the anti-Hr sera. These ambiguous reactions are due to the inclusion in the phenotypes of more than one genotype. There are 36 possible genotypes, and these are distributed numerically among the phenotypes in the following way: 1, 2, 2, 2, 5, 5, 5, 14 in the order given in Table II.

TABLE II.

The Rh Phenotypes and their Reactions with Antisera.

Phenotype.		Reaction with Anti-Rh Sera.			Possible Genotypes[2] (Using the Suggested Nomenclature of Graydon and Simmons).	Reactions with Anti-Hr Sera.		
Graydon and Simmons.	Wiener.[1]	Anti-Rh^0.	Anti-Rh^1.	Anti-Rh^2.		Anti-Hr^0.	Anti-Hr^1.	Anti-Hr^2.
Rh-negative (rh)	Rh-negative	−	−	−	rr	+	+	+
Rh^0	Rh$_0$	+	−	−	R^0R^0 R^0r	− +	+ +	+ +
Rh^1	Rh′	−	+	−	R^1R^1 R^1r	+ +	− +	+ +
Rh^2	Rh″	−	−	+	R^2R^2 R^2r	+ +	+ +	− +
Rh^{01}	Rh$_1$	+	+	−	$R^{01}R^{01}$ $R^{01}R^0$ $R^{01}R^1$ $R^{01}r$, R^0R^1	− − + +	− + − +	+ + + +
Rh^{02}	Rh$_2$	+	−	+	$R^{02}R^{02}$ $R^{02}R^0$ $R^{02}R^2$ $R^{02}r$, R^0R^2	− − + +	+ + + +	− + − +
Rh^{12}	Rh′Rh″	−	+	+	$R^{12}R^{12}$ $R^{12}R^1$ $R^{12}R^2$ $R^{12}r$, R^1R^2	+ + + +	− − + +	− + − +
Rh^{012}	Rh$_1$Rh$_2$	+	+	+	$R^{012}R^{012}$ $R^{012}R^{01}$ $R^{012}R^{02}$ $R^{012}R^{12}$ $R^{012}R^0$, $R^{01}R^{02}$ $R^{012}R^1$, $R^{01}R^{12}$ $R^{012}R^2$, $R^{02}R^{12}$ $R^{012}r$, R^0R^{12}, R^1R^{02}, R^2R^{01}	− − − + − + + +	− − + − + − + +	− + − − + + − +

[1] Since the preparation of this paper and Tables I, II and IIA, Wiener (personal communication) has advised us of two changes in his phenotype nomenclature; Rh-negative becomes rh, and Rh_0 becomes rh_0. In his genotype nomenclature he has dropped the "h" and he now uses superscripts only, for example, rr, R^1R^1, R^1r^0 *et cetera*.

[2] This includes the genotypes for the rare gene Rh_Z (R^{015}) and the predicted gene Rhy (R^{115}), also the reactions with the predicted anti-Hr serum.

TABLE IIA.

Phenotype.		Reaction with Antisera.				Possible Genotypes.
Graydon and Simmons.	Wiener.	Anti-Rh^0.	Anti-Rh^1.	Anti-Rh^2.	Anti-Hr^1.	
Rh-negative (rh)	Rh-negative	−	−	−	+	rr
Rh^0	Rh$_0$	+	−	−	+	R^0R^0, R^0r
Rh^1	Rh′	−	+	−	− +	R^1R^1 R^1r
Rh^2	Rh″	−	−	+	+	R^2R^2, R^2r
Rh^{01}	Rh$_1$	+	+	−	− +	$R^{01}R^{01}$, $R^{01}R^1$ $R^{01}r$, $R^{01}R^0$, R^0R^1
Rh^{02}	Rh$_2$	+	−	+	+	$R^{02}R^{02}$, $R^{02}R^2$, $R^{02}r$, $R^{02}R^0$, R^0R^2
Rh^{12}	Rh′Rh″	−	+	+	− +	$R^{12}R^{12}$, $R^{12}R^1$ $R^{12}R^2$, $R^{12}r$, R^1R^2
Rh^{012}	Rh$_1$Rh$_2$	+	+	+	− +	$R^{012}R^{012}$, $R^{012}R^{01}$, $R^{012}R^{12}$, $R^{012}R^1$, $R^{012}R^{12}$ $R^{01}R^{02}$, $R^{01}R^2$, $R^{02}R^1$, $R^{012}R^{02}$, $R^{012}R^0$, $R^{012}R^2$, $R^{012}r$, $R^{02}R^{12}$, $R^{12}R^0$

It is not considered that any more detailed and descriptive terminology for the phenotypes would be justified, as the one suggested completely outlines the reactions with the three known anti-Rh sera. The extension of the nomenclature of the phenotypes in order to give the reactions with all six types of serum (the letter "H" with suitable superscripts could be used for this purpose) would require 27 different designations, and even these would not be enough to determine all of the genotypes involved. There would still be six phenotypes with two genotypes each and one phenotype with four possible genotypes (see Table II).

One desideratum in the naming of human phenotypes, particularly those of clinical importance, is that the terminology adopted should not be cumbersome when used orally. This is an important disadvantage in the "capital *C*—small *c*" usage. In our suggested series Rh^{o} is pronounced Rh "oh one".

Because superscripts and subscripts cannot be readily distinguished when spoken, superscripts have been adhered to throughout. (The generally accepted practice in modern genetics is to use superscripts only for alleles occupying the same locus.)

The comments which have been made on Wiener's nomenclature for the genes apply equally well to his phenotypes. In addition it is pointed out that Wiener's "double acting" phenotypes $Rh'Rh''$ and Rh_1Rh_2 may be confused with genotypes. One would naturally expect the Rh_1Rh_2 phenotype to contain a double dose of the Rh^{o} antigen, as it appears to be a combination of the Rh_1 and Rh_2 genes, both of which contain the Rh^{o} antigen. This is the case only with some of the cells classed in the Rh_1Rh_2 phenotype.

The Rh Antisera.

In the naming of the anti-Rh sera, the designations of Wiener have been adhered to except in the substitution of the superscripts "1" and "2" for the "prime" and "double prime" respectively, and in the use of the superscript "0" in "anti-Rh^{o}". No other alteration appears to be desirable. The use of numbers 1 to 6 as suggested by Murray could be justified only if his genetic terminology, which is not generally favoured, was accepted.

The Greek letters suggested by Fisher seem to introduce an additional factor confusing to many workers. The letters *C*, *D*, *E* and *c*, *d*, *e* are rather cumbersome when used orally. However, it seems to us that six only of the twelve symbols are necessary, for the antisera might be satisfactorily identified by the use of "anti-" preceding the name of the corresponding antigen—for example, *D* and anti-*D*, and Δ (or δ) and anti-Δ (or δ) for the corresponding Hr serum; or, if preferred, *D* and anti-*D*, and *d* and anti-*d*. If it was shown that the six antigens collectively known as the Rh factor were actually associated with three loci which are not completely linked, it might be desirable to continue the use of such letters (*C*, *c*, *D*, *d*, *E*, *e*), which have a definite advantage when one is describing such factors as the "Willis" antigen reported by Callender *et alii* (1945).

Rh antisera which react in the same way as the original anti-rhesus serum of Landsteiner and Wiener have generally been referred to as standard anti-Rh sera. It is suggested that the term "standard" is no longer necessary in this connexion, and may for reasons given below lead to confusion.

The Hr Antisera.

Wiener (1945) has also proposed that Hr antisera which give the same specific reactions as Race and Taylor's "St" serum should be referred to as standard anti-Hr sera, priority thus being given to the Hr name of Levine and Javert (Levine, 1943). There seems to be no need to use the term "standard", and it may cause confusion for the following reasons: (i) There is no reciprocal relationship between the so-called "standard Rh antiserum" and the "standard Hr antiserum", the former being anti-Rh^{o} and the latter anti-Hr^{1} serum. (ii) The term "standard" may well be required for use when Rh and Hr sera are placed on a suitable basis with regard to potency. It may eventually be possible to prepare standard sera, either in liquid or in dried form, with which the potency of other Rh and Hr antisera can be compared.

In naming the anti-Hr sera we have used superscripts as in the corresponding anti-Rh sera; thus we have "anti-Hr^{o}", "anti-Hr^{1}" and "anti-Hr^{2}" respectively.

The Reactions of Genes with Rh and Hr Antisera.

From Table I it may be seen that each gene reacts either with a particular anti-Rh serum or with its corresponding Hr antiserum, but never with both. This fact has been utilized by Wiener (1945) in a neat method evolved for forecasting the percentage of positive reactions which any particular Hr type of serum will give in a homogeneous population, when the percentage of positive reactions with the corresponding Rh type serum is known.

Each anti-Rh and anti-Hr serum pair react in much the same way with blood samples as do the M and N type antisera, and the cells can thus be classified as homozygous or heterozygous with respect to this pair; for example, anti-Rh′ serum and anti-Hr′ serum may be used to test a number of samples of cells, and from their reactions three groups may be obtained—namely, those reacting with anti-Rh′ serum only, those reacting with both antisera and those reacting with anti-Hr′ serum only. The statistical treatment of these reactions is identical with that for the M,N system. It may be easily deduced (formula (I)) that:

$$Hr'+ = 1 - (1 - \sqrt{Rh'-})^2$$

Thus, from a knowledge of the percentage of positive reactions given by any anti-Rh serum in a homogeneous population, the percentage of positive reactions given by the corresponding Hr antiserum may be calculated (see Table III).

Table III.

Showing the Expected Percentage of Positive Reactions with any Hr Antiserum when the Percentage of Positive Reactions with the Corresponding Rh Antiserum is Known (or Vice Versa).

Rh+	Hr+	Rh+	Hr+	Rh+	Hr+
100	—	90	53	80	69
99	19	89	55	79	71
98	26	88	57	78	72
97	33	87	59	77	73
96	36	86	61	76	74
95	40	85	62 (5)	75	75
94	43	84	64		
93	46	83	65 (5)		
92	49	82	67		
91	51	81	68		

It is obvious from Table III that formula (I) is of little value in predicting reactions of Hr serum when the percentage of positive reactions with the Rh serum is greater than 95%. Conversely, if the percentage of positive reactions is comparatively low with the Rh serum, the percentage of positive reactions with the Hr serum can be accurately forecast. The same statistical tests used for the M,N system may be applied to the three separate Rh-Hr systems, for it is easy to show that $\sqrt{Rh'-} + \sqrt{Hr'-}$ should be equal to 1·0, and its deviation from unity in any particular sampling has the standard error

$$\sigma_D = \frac{1}{2\sqrt{V}}$$

where *V* is the number of samples examined. The values of *D* and σ_D have been calculated for some of the published and unpublished data on different races, and are given in Table IV, from which it may be seen that the figures fit the theory remarkably well.

To date, Fisher's theory has proved adequate in explaining the genetic relationships of the Rh agglutinogens; but as knowledge of this complex genetic system is extended, it may become necessary to modify these conceptions. It is, therefore, important that the notation finally adopted should be simple, descriptive and capable of extension. The nomenclature suggested in the foregoing fulfils these requirements, and further, its departure

TABLE IV.

Application of the Statistical Tests to the Percentage of Positive Reactions Obtained in the Rh^1-Hr^1 System in Various Races.

Population Studied.	Authors.	Number of Samples Tested.	Percentage of Positive Reactions with Antisera.		D	σ_D	D/σ_D
			Anti-Rh^1.	Anth-Hr^1.			
Australian whites	Simmons *et alii* (1945).	225	72·4	76·0	0·015	0·03	0·5
English	Fisher and Race (1946).	927	69·26	80·15	0·00002	0·017	<0·1
Mexican Indians	Wiener *et alii* (1945).	95	89·5	55·8	0·01	0·05	0·2
Papuans	Simmons *et alii* (1946).	100	100·0	8·0	0·04	0·05	0·8
Indonesians	Present authors (in preparation).	100	96·0	33·0	0·02	0·05	0·4
Fijians	Present authors (in preparation).	110	98·2	29·1	0·02	0·05	0·4
Melanesians (Admiralty Islands)	Present authors (in preparation).	112	99·1	12·5	0·03	0·05	0·6
American whites	Wiener (personal communication).	645	69·0	79·3	0·012	0·02	0·6

from the original suggestions of Wiener all tend to aid the novice in understanding the reactions of the system, while the changes made present no difficulties to those familiar with the genetics of Rh.

SUMMARY.

1. A brief descriptive introduction covering certain milestones in the development of knowledge of the Rh blood types is given.

2. The reactions of the eight Rh genes and of eight of the Rh phenotypes with the six type antisera are presented in tabular form. The possible genotypes pertaining to each phenotype are also given.

3. A suggested scheme for the nomenclature of the Rh genes, phenotypes and type specific antisera is proposed. This scheme is held to be simple, easily memorized, unambiguous in oral use and descriptive of the reactions of the genes with the type-specific antisera.

4. Some statistical considerations relating to the Rh and Hr systems in racial studies are discussed.

BIBLIOGRAPHY.

S. Callender, R. R. Race and Z. V. Paykoc: "Hypersensitivity to Transfused Blood", *British Medical Journal*, Volume II, July 21, 1945, page 83.

R. A. Fisher and R. R. Race: "Rh Gene Frequencies in Britain", *Nature*, Volume CLVII, January 12, 1946, page 48.

K. Landsteiner and A. S. Wiener: "An Agglutinable Factor in Human Blood Recognized by Immune Sera for Rhesus Blood", *Proceedings of the Society for Experimental Biology and Medicine*, Volume XLIII, 1940, page 223; "Studies on an Agglutinogen (Rh) in Human Blood Reacting with Anti-Rhesus Sera and Human Isoantibodies", *The Journal of Experimental Medicine*, Volume LXXIV, 1941, page 309.

P. Levine and R. E. Stetson: "An Unusual Case of Intra-group Agglutination", *The Journal of the American Medical Association*, Volume CXIII, 1939, page 126.

P. Levine, L. Burnham, E. M. Katzin and P. Vogel: "The Role of Isoimmunization in the Pathogenesis of Erythroblastosis Fetalis", *American Journal of Obstetrics and Gynecology*, Volume XLII, 1941, page 925.

P. Levine: "The Pathogenesis of Fetal Erythroblastosis", *The New York State Journal of Medicine*, Volume XLII, 1942, page 1928; "The Pathogenesis of Erythroblastosis Fetalis", *The Journal of Pediatrics*, Volume XXIII, 1943, page 656.

A. E. Mourant: "A New Rhesus Antibody", *Nature*, Volume CLV, 1945, page 542.

J. Murray: "A Nomenclature of Subgroups of the Rh Factor", *Nature*, Volume CLIV, December 2, 1944, page 701.

J. Murray, R. R. Race and G. L. Taylor: "Serological Reactions Caused by the Rare Gene Rh_s", *Nature*, Volume CLV, 1945, page 112.

R. R. Race and G. L. Taylor: "A Serum that Discloses the Genotype of some Rh-Positive People", *Nature*, Volume CLII, 1943, page 300.

R. R. Race: "An 'Incomplete' Antibody in Human Serum", *Nature*, Volume CLIII, 1944, page 771.

R. R. Race, G. L. Taylor, E. W. Ikin and A. M. Prior: "The Inheritance of Allelemorphs of the Rh Gene in Fifty-Six Families", *Annals of Eugenics*, Volume XII, 1944, page 206.

R. T. Simmons, Rachel Jakobowicz and G. A. Kelsall: "The Rh Factor: A Survey of the Subtypes of White Australians", THE MEDICAL JOURNAL OF AUSTRALIA, December 29, 1945, page 493.

R. T. Simmons, J. J. Graydon and E. F. Woods: "Further Observations on the Rh and Hr Factors, and the Blood Group Frequencies in Papuans", THE MEDICAL JOURNAL OF AUSTRALIA, April 20, 1946, page 537.

L. H. Snyder: "The Nomenclature of the Rh Blood Types", *Science*, Volume CI, January 19, 1945, page 62.

A. S. Wiener and H. R. Peters: "Hemolytic Reactions following Transfusions of Blood of the Homologous Group, with Three Cases in which the Same Agglutinogen was Responsible", *Annals of Internal Medicine*, Volume XIII, 1940, page 2306.

A. S. Wiener: "Hemolytic Reactions following Transfusions of Blood of the Homologous Group", *Archives of Pathology*, Volume XXXII, 1941, page 227; "Genetic Theory of the Rh Blood Types", *Proceedings of the Society for Experimental Biology and Medicine*, Volume LIV, 1943, page 316; "Theory and Nomenclature of the Hr Blood Factors", *Science*, Volume CII, November 9, 1945, page 479.

A. S. Wiener, J. P. Zepeda, E. B. Sonn and H. R. Polivka: "Individual Blood Differences in Mexican Indians, with Special Reference to the Rh Blood Types and Hr Factor", *The Journal of Experimental Medicine*, Volume LXXXI, 1945, page 559.

EARLY DIAGNOSIS IN TUMOURS OF THE CENTRAL NERVOUS SYSTEM.

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TUMOURS of the central nervous system have always been the most serious problem that is presented to the neurosurgeon, and by the term tumour I mean all types of expanding lesion, such as neoplasm, abscess, cyst, hæmorrhage and the like. It was not so many years ago that tumours of the central nervous system, especially neoplasms, were regarded by surgeons as lesions of considerable clinical and pathological interest, but purely from an academic point of view. Those who were courageous enough to attempt removal had an extremely high operative mortality rate. As a result of the pioneering work of Harvey Cushing and his colleagues, the operative removal of cerebral and spinal tumours became a definite science and mortality figures dropped from the 80% to 90% mark to 10% to 15%. This remarkable reduction was mainly due to more accurate methods of localization, such as encephalography, to a greater knowledge of neuropathology, and to improved methods of operative technique, so that previous methods of opening the skull on chance were no longer necessary.

The next and more important step in the progress of neurosurgery was to convince the medical profession that neurosurgery with regard to tumours was no longer a eulogistic fugue on the part of a few enthusiastic visionaries, but a very real procedure that could rehabilitate many of these patients for varying periods of time, according to the nature and site of the lesion. This object has largely been achieved. With the aid of experience, further improvements in methods of localization and operative technique, and a greater knowledge of neuro-anatomy, neurophysiology and neuropathology, we have been able to reduce the operative mortality rate to about 4% to 5% and the total case mortality rate to 10% to 15%.

On going through my own records I have noticed one outstanding point. In practically every case in which death

occurred, the patient exhibited advanced signs of increased intracranial pressure by the time he was admitted to hospital. In some instances an operation was performed merely in the rather forlorn hope that some improvement might be obtained. In others any attempt at operative removal of the lesion was regarded as being out of the question. In a number of these cases it was apparent that, had the lesion been recognized years, months or even weeks earlier, temporary or permanently good results could have been obtained. And this point brings me to the object of presenting this paper and the vital necessity for early recognition of any type of expanding lesion of the central nervous system. This is, of course, applicable to practically all bodily tumours; but whereas a lesion may expand to an enormous size in other parts of the body without interfering with function, the central nervous system is enclosed within a bony compartment—namely, the skull and spinal column—which is solid and contains very little free space to accommodate extraneous growths of an expansile nature. Consequently, after a certain stage, further expansion of the lesion must take place at the expense of the normal cranial or spinal contents either by displacement or replacement.

In presenting this paper I have very little that is new or original to offer, nor do I write with the object of exhibiting my limited knowledge and neurosurgical results. I realize the difficulties of the general physician and surgeon, who must keep abreast with the times in all branches of medical literature, with the result that the relatively uncommon surgical lesions of the central nervous system must often take a back seat in favour of the more common bodily diseases. Also, I do sincerely request that those readers who have paid me the compliment of referring to me the cases presented do not regard this paper in the light of a destructive criticism. It is written purely as an effort to present the more important symptoms and signs of intracranial expanding lesions in an abbreviated form, so that it may assist the practitioner to recognize the presence of these lesions as soon as possible after the onset of the symptoms.

These symptoms and signs can be roughly divided into two main groups. General symptoms and signs, such as headache, lassitude, drowsiness and papilœdema, are usually the result of increased intracranial pressure. Focal symptoms and signs, such as paralysis, ataxia, dysphasia and anæsthesia, are usually due to direct involvement of the central area controlling these functions or of the cerebro-spinal pathways. General symptoms are of value in suggesting or indicating the presence of an expanding lesion of the central nervous system, while focal symptoms or signs aid in the localization of such a lesion to one particular part. The old triad of headache, vomiting and papilœdema is truly an indication of increased intracranial pressure, but at this stage it is frequently too late to attempt any surgical removal. Tumours of the spinal cord rarely attain a large size before producing fairly definite localizing symptoms and signs; but such lesions may exist and expand to relatively large proportions in certain areas of the brain without causing the patient any discomfort.

In the following case a perfect result was obtained in spite of the relatively long history. This was mainly due to the fact that there was no evidence of cerebral dysfunction as the result of increased intracranial pressure.

CASE I.—Mr. B.B., aged forty-two years, complained of a small lump in his right frontal region. This lump had been present for eighteen months and was gradually increasing in size and had become tender during the past three days. Flat X-ray plates were sufficient to confirm the original impression of a meningioma. At operation the tumour measured about 5·5 centimetres in diameter and occupied the whole of the right frontal area, having displaced the brain backwards. Although the tumour tissue had invaded and filled the frontal sinus, a complete removal was possible, and the patient made an uninterrupted recovery and was ready for discharge from hospital on the tenth day.

Obviously, in such cases it may be impossible even to suspect the presence of a tumour, so it is all the more vital that such a lesion should be detected soon after the appearance of the first outward sign. In the case of any expanding lesion, irrespective of its pathological nature or of what the early symptom or sign may be, the point that gives us the greatest concern is the progressive nature of that symptom or sign. A good rule to follow is to regard any neurological symptom or sign that becomes progressively worse as a definite indication for further specialized investigation. In the following paragraphs are set out in an abbreviated form the main features of the usual procedure that is carried out in the investigation of neurological conditions.

Subjective Symptoms.

A careful history will often suggest the possibility of an intracranial expanding lesion. Particular attention should be paid to the length of time for which the symptoms have been present and whether they are becoming progressively worse. The age of the patient is important, as progressive symptoms commencing in later life are more suggestive of an expanding lesion than those starting in youth. Conversely, symptoms that have been present for many years and which are not progressive in nature are not likely to be associated with a tumour. If there is the slightest doubt, it is always wise to protect oneself by having ventricular air studies carried out so that a tumour can be excluded.

Headache.

Headache is one of the earliest symptoms associated with intracranial and sometimes with intraspinal tumours. It may result from increased intracranial pressure or from direct pressure by the lesion on one or other of the pain-sensitive structures within the skull. Pain-sensitive structures above the tentorium are supplied from the trigeminal (or fifth cranial) nerves, the fibres from which mainly accompany the larger blood vessels. These pain-sensitive structures are the internal carotid arteries and their larger branches, the meningeal arteries, the dural blood sinuses and the larger cortical veins as they approach the sinuses, while the dura proper and the brain substance are quite insensitive. Consequently, headache arising from a lesion above the tentorium is referred to the anterior half of the head in front of a vertical plane through the ears. Infratentorial structures receive their nerve supply from the glosso-pharyngeal and vagus (or ninth and tenth cranial) nerves and possibly from the upper three cervical nerves, so that lesions below the tentorium may produce headache which is referred to the posterior half of the head behind the vertical plane through the ears. Thus it can be seen that headache is rarely of assistance as a localizing sign unless it is unilateral, although headache from an infratentorial lesion may be confined to the suboccipital region at the onset. In the early stages the headache is intermittent, but it later becomes more frequent, more prolonged and more severe. It may be described as throbbing or bursting in character and may become worse on coughing, straining or excitement or when the patient is lying in the prone position.

Epileptiform Seizures.

Epileptiform seizures are so commonly associated with intracranial tumours, often as the initial symptom, that every patient suffering from seizures of any type should be regarded as a tumour suspect and should have a complete and careful neurological investigation. This would appear to be rather a broad statement; but the more I see of these cases, the more I realize its truth. This is more important as the age of onset increases, and particularly if there is any evidence of a focal nature in the pattern of the attack. With regard to patients who have a long history, or who give a history of similar seizures in other members of the family, or, in fact, all patients without any focal signs up to the age of fourteen years, I feel that a more conservative attitude may be adopted and a trial with medication is permissible. These patients should be kept under constant observation, as occasionally a tumour has been found in such cases, and also there is no reason why a primary epileptic should not develop a tumour.

Every effort should be made to obtain an accurate account of a seizure from the patient and from observers, as some information of localizing value may be elicited. It is amazing how few people, even when medically

trained, are able to give a concise chronological account of an epileptiform seizure. In most cases the bystanders are so busy rushing about frantically or sitting on top of the patient to hold him down, instead of letting him have his fit in peace, that much valuable information is lost. When obtaining a history one should beware of inaccurate observations. The observer should be questioned again and again, and if there is the slightest doubt on any point that point should be completely disregarded, as it would be tragic to open a skull on the basis of inaccurate information. The motor and sensory phenomena that occur within the first few seconds of the attack are of greatest localizing value, as they indicate the firing point in the cerebral cortex from which the attack originates. Thus it can be seen that the so-called aura is not really a warning of an oncoming attack, but, in reality, the beginning of the attack itself.

An epileptic fit or seizure is really the outward manifestation of a cerebral dysrhythmia that commences at one or more points in the brain and spreads outwards like a radio wave or the ripple on a pond when a pebble is thrown into the water. As this march of abnormal neuronal impulses spreads, and various adjacent areas become involved, there is a corresponding march of sensory or motor phenomena that may be experienced by the patient or seen by an observer. In many cases this march may be so rapid that the component parts are not apparent, and the patient may simply utter a cry and fall down unconscious in a generalized seizure. It should be realized that, in cases of tumour, the seizures do not originate from the actual tumour cells, but from the neighbouring damaged cortical nerve cells. The following is a composite account of one type of focal attack, and it includes the more important points that should be inquired into by the medical examiner.

PATIENT: I always get a warning for about a minute before the fit by a feeling of numbness and tingling that starts in the tips of the fingers of my right hand, then my fingers start to twitch and the elbow and shoulder begin to jerk, and that is all I remember. When I come out of it I feel very tired and my right hand is weak for half an hour or so, then I am quite normal again.

OBSERVER: At the beginning of each attack I notice a queer expression on his face, and about thirty seconds later the fingers of his right hand begin to twitch. Within a further thirty seconds this twitching spreads to his forearm and shoulder. His head turns to the right, the right side of his face twitches, and he falls down unconscious, usually to the right side. I quickly lay him on his back, loosen his tie and collar to give him a free airway, and place half a clothes peg wound round with a piece of cloth between his teeth. By this time the convulsive seizures become generalized, but more marked on the right side, the left side being more rigid. He froths at his mouth and his face becomes blue, particularly around the mouth. He doesn't breathe much during the attack, but his breathing is deep and laboured when the convulsions stop. The convulsions last about one and a half to two minutes and then he gradually becomes conscious. His right hand is definitely weak for half an hour or so afterwards. He has occasionally lost control of his bladder and bowels during the attack. He has bitten his tongue and cheek on previous occasions before we started using the clothes peg.

This is, of course, a purely hypothetical description, which one always hopes to obtain instead of having to ferret out the details one by one. It gives the march of sensory and motor phenomena from a firing point situated about one inch above the left ear in the post-central cortex. It also demonstrates the correct management during a seizure. Such actions as holding the patient down, plunging him into a hot mustard bath, applying hot or cold packs, blankets *et cetera*, are entirely incorrect, as any interference only tends to act as an irritant and prolong the attack. Seizures arising from other cortical areas would have corresponding differences in their pattern.

It must be realized that only a relatively small number of epileptic patients are suffering from tumours. In the majority of cases there is no apparent cause, and these types of epilepsy have received various names, such as idiopathic, essential or cryptogenic epilepsy. In such cases an attack may start from a single firing point and have an extremely rapid spread, or it may originate from several scattered firing points throughout the brain. In either case no focal evidence is apparent to an observer. This, however, does not eliminate the presence of an expanding lesion, which frequently produces a seizure of a type without any evidence of a focal nature. In summarizing the relative importance of seizures with regard to tumours, I should like to stress forcibly the vital necessity for complete neurological investigation (including encephalography) of all epileptic patients who show any focal evidence in the pattern of their attack. In all cases in which the onset is after the age of about fourteen to sixteen years, such an investigation should be made. Patients with a long history or with an onset before the age of fourteen years can first be treated medically with safety, providing their attacks are not focal. They must be kept under constant observation, and the slightest sign of a progressive nature should be regarded as an indication for further investigation. One must be careful not to give way to wishful thinking after the first seizure We are very apt to compromise, especially when the patient or parents are apprehensive of any investigation, and adopt a "wait and see" attitude. This is dangerous, as the interval between the first and second attacks due to a tumour may be as long as one or more years. It is far better that many should be subjected to the expense and discomfort of a complete investigation than that one should die because that investigation was not carried out or was delayed.

The following case illustrates the tragedy of not carrying out ventricular air studies in a case of focal epilepsy starting late in life. If the condition had been recognized in the early stages, a good result might have been obtained.

CASE II.—Mr. P.N., aged forty-five years, complained of epileptiform seizures of four years' duration. Most of these attacks had a focal pattern, in that the movements were confined to the left arm and leg. When I first examined him, slowing of cerebration and mental confusion and a left hemiparesis were present. Ventriculographic examination revealed a large right parietal expanding lesion. At operation the outline of a large, solid tumour could be felt with the brain needle. As the tumour was deep and almost certainly involved the *corpus callosum*, no attempt was made to remove it. A subtemporal decompression operation was carried out purely as a palliative measure. The patient improved for a few days, but his condition became rapidly worse and he died.

Vomiting.

Vomiting rarely occurs in the early stages, but it is frequently encountered in the later stages when the intracranial pressure becomes high, and it is usually associated with severe headache. Intermittent attacks of headache and vomiting, which may be relieved by lying down or suddenly changing the position of the head, are suggestive of a third ventricle cyst which happens to obstruct the flow of cerebro-spinal fluid until it is dislodged. Vomiting may sometimes be projectile in nature, but this is much less common than was formerly supposed.

Ataxia.

Ataxia may be a predominant symptom in various diseases of the central nervous system, but progressive ataxia should always be investigated to exclude an expanding lesion. True ataxia is usually due to some interference with the function of the cerebellum or labyrinths, and such dysfunction may be caused by a tumour. Tumours of the frontal lobe may produce symptoms and signs characteristic of a cerebellar tumour, and such lesions must be localized accurately by ventricular air studies, as the result is likely to be fatal if a suboccipital craniotomy is performed in a case in which a supratentorial expanding lesion is present. Tumours involving the post-central cortex may produce a pseudo-ataxia. In these cases the incoordination of movement is due to loss of deep joint position sense, and is greatly exaggerated when the eyes are closed, whereas true ataxia is not increased to such an extent when the assistance of vision is eliminated.

Vertigo.

Occasionally vertigo may be associated with increased intracranial pressure, and is probably due to interference with the blood circulation in the labyrinths.

Dysphasia.

Various forms of dysphasia may be met with in cases of cerebral tumour, according to which part of the speech-controlling cortex is involved. Lesions of the motor speech or Broca's area produce a dysphasia in which the patient knows what he wants to say but is unable to speak the words or sentence. Such patients can recognize objects and will agree when the correct name is spoken by the examiner. Emotional speech in such cases is much less affected, and the patient may be able to swear quite fluently while being otherwise speechless. This is termed verbal or motor dysphasia. Writing is similarly affected, in that the patient can think quite clearly, but is unable to translate his thoughts into writing. Nominal dysphasia is an inability to name objects correctly, although the patient may be able to demonstrate the use of the object. For example, he may go through the motions of writing when presented with a pencil or a pen although unable to name the object. This may occur in lesions near the angular gyrus or in the temporal or frontal lobes. Jargon dysphasia is sometimes associated with lesions of the posterior part of the temporal lobe, and the term is in itself descriptive, in that the patient may talk quite volubly and pour out a stream of meaningless words or sounds. Word-blindness or visual dysphasia is an inability to comprehend written words or sentences, and may occur in lesions of the left parieto-occipital cortex. Similarly, word deafness or auditory dysphasia is an inability to comprehend spoken words and may result from lesions of the left temporal lobe.

Mental Symptoms.

I should like to emblazon the two words "mental symptoms" across this page in letters of fire, so important is their association with cerebral tumours. In all cases in which mental disturbance is present, whether it be neurosis, hysteria or true insanity, one should keep in mind the possibility of an intracranial expanding lesion. Each case should be gone into thoroughly with a careful history and examination, and unless a definite psychopathic diagnosis can be made, encephalography should be performed to eliminate a tumour. Mental symptoms may be caused by direct involvement of the *corpus callosum* or frontal lobes or by increased intracranial pressure due to tumours in other situations. They usually begin with vague abnormalities of behaviour, impairment of memory and slowing of cerebration, leading to progressive dementia with personal carelessness and incontinence of the sphincters. I believe it is wise, in all cases of progressive dementia occurring in previously normal people, to regard those people as tumour suspects and to carry out ventricular air studies.

The following case contains a dual object lesson. The patient's hysterical symptoms masked an underlying cerebral tumour. I had labelled her condition as functional, and I did not see fit to review this decision until it was almost too late.

CASE III.—Miss V.B., aged forty-five years, was first examined by me in 1942. She complained of deterioration of memory of twelve months' duration and of seizures of five months' duration. She had suffered from poliomyelitis at the age of six years, and had a pronounced residual defect in both legs and the left arm; bilateral ankle ankylosis had been performed. She was admitted to hospital immediately as a tumour suspect. Ventricular air studies revealed only slight abnormality. She had a "seizure" in my presence, which was obviously hysterical, and which she stated was similar to the previous attacks. Neurological examination gave confusing results because of the hysterical element and the poliomyelitis lesions. She was regarded as suffering from pure hysteria and treated accordingly, mainly by painful electrical stimulation of the left arm and leg and verbal encouragement. After this she lost all her symptoms and was discharged from hospital feeling well.

During the following three years she consulted other doctors for different symptoms which varied considerably in type and severity. Three of these doctors called me in consultation, as each felt that all her symptoms were not functional and that there was some underlying organic lesion. Unfortunately I was biased beforehand and still regarded her condition as purely functional, until finally I realized that possibly the others were right and I was wrong. She was readmitted to the Royal Prince Alfred Hospital, and ventricular air studies then revealed a right parasagittal expanding lesion. This proved to be a large meningioma and was successfully removed at operation. She is now perfectly well physically, but still has pronounced weakness of her left arm and leg.

The lesson to be learnt from this case is that the patient was pigeon-holed as suffering from a functional condition, whereas she should have been discharged from hospital as a tumour suspect and readmitted in six months' time for further ventricular air studies. If operation had been carried out earlier, almost certainly the weakness of her left arm and leg would have been avoided.

The next case illustrates the point that an hysterical patient may subsequently develop an intracranial expanding lesion.

CASE IV.—Mr. T., aged forty-five years, complained of loss of use in his legs, and of attacks in which both his legs shook violently. I saw him in consultation with two other honorary medical officers, and we all agreed his condition was entirely functional. A full-volume encephalogram was done as a therapeutic measure, and the X-ray films revealed a well-filled and perfectly normal ventricular system. About six weeks later he was readmitted to hospital with similar symptoms. While in hospital he had a sudden left hemiplegia, which was certainly organic in origin. Ventricular air studies revealed a large right parietal tumour. The lesion was regarded as a rapidly growing and inoperable *glioblastoma multiforme*. This impression was later confirmed at autopsy.

General Symptoms and Signs.

Evidence of glandular dyscrasia such as adiposity, interference with menstruation, growth of superfluous hair, excessive thirst and polyuria should lead one to suspect an intracranial lesion. If a tumour is the cause, it is usually in the form of a pituitary adenoma or a craniopharyngioma; but tumours elsewhere within the cranium may produce these symptoms indirectly through increased intracranial pressure. Pineal tumours are fortunately rare, and they also cause growth and developmental abnormalities. X-ray evidence of an enlarged pituitary fossa would suggest a pituitary tumour while calcification above the sella would suggest a craniopharyngioma. If a bitemporal defect is found on examination of the visual fields, together with an enlarged sella, a pituitary tumour is almost certainly present, although a craniopharyngioma may occasionally cause field defects. The visual fields should always be examined carefully on a proper perimeter, as minor peripheral defects may be missed in crude confrontation tests or on a flat screen. In fact, visual field examination should be made by an ophthalmologist, unless the examiner is accustomed to the procedure, as it is highly technical and fraught with difficulties.

Objective Findings.

Septic Foci.

A thorough search should be made for septic foci, especially in the teeth, tonsils, sinuses, ears and lungs, as various neurological lesions may result from toxic absorption from such foci. Toxic cerebral œdema is the main lesion which simulates an expanding lesion and this condition is in reality a diffuse expanding lesion, comparable to an *astrocytoma diffusum*, which can cause severe headache and vomiting, elevate the cerebro-spinal fluid pressure to that of 500 millimetres of water or more, and produce intense papilloedema of several diopters. It is due to an interference with the water-balance mechanism, with a resultant pronounced increase in the intracellular and interstitial fluid. In these cases there are usually no localizing signs, and a tumour can only be excluded by ventricular air studies. Cerebral or spinal abscess may result from direct or metastatic spread from a primary infective focus.

Extracranial Newgrowths.

Extracranial newgrowths will, of course, be searched for in the general examination. If an intracranial tumour is present, it is a good plan to have an X-ray examination of the chest made as cerebral metastatic carcinoma is frequently the result of spread from a primary growth in the lungs. As such cerebral deposits are often multiple,

it is questionable whether it is justifiable to remove the obvious cerebral lesion. Tumours of the skin may give one a lead in the presence of neurological symptoms. Neurofibromatosis is not infrequently associated with similar tumours connected with the spinal nerves or the auditory nerves, and lipomata are occasionally met with in a similar manner.

Blood Pressure.

Headache and dizziness are common symptoms in essential and arteriosclerotic hypertension, and the optic disks may have an appearance similar to that in true papillœdema. Progressive dementia may be due to cerebral arteriosclerosis; but the presence of an expanding lesion can be excluded only by encephalography. The blood pressure may rise in cases of cerebral tumour, but only in the terminal phases.

Head.

External examination of the head may elicit valuable information. A hard bony lump, slowly increasing in size, would suggest the presence of an underlying meningioma, and such a lump may be tender on pressure. An intracranial bruit may be heard with the stethoscope over a vascular tumour or angioma, and occasionally in the presence of an aneurysm. Congestion of the scalp veins and arteries should lead one to suspect the presence of increased intracranial pressure. Arterial congestion is usually confined to the same side as the lesion. In children, before the suture lines close, increased intracranial pressure may reveal itself by an increased size of the head, separation of the suture lines, a "cracked pot" sound on percussion or congestion of the scalp veins.

The Cranial Nerves.

First Cranial Nerve.—Interference with the sense of smell may occur in tumours involving the olfactory tracts, especially in meningiomata of the olfactory groove. A tumour near the uncinate gyrus may reduce the sense of smell in the ipsilateral nostril, or it may produce olfactory hallucinations. Uncinate fits are so called because they are heralded by an unpleasant aroma.

Second Cranial Nerve.—The visual acuity is tested by means of a chart. All cases of progressive deterioration of vision should be fully investigated for cerebral tumour, as this may be the first and only symptom when the patient reports to his doctor. Loss of vision in the presence of a cerebral tumour is usually due to papillœdema, although it may occur from primary atrophy due to direct pressure on the optic nerve by the lesion. If papillœdema is allowed to exist too long without relief, a secondary optic atrophy develops with further loss of vision advancing to complete blindness, which will not recover even after the causative lesion is successfully removed. Papillœdema is believed to be due to obstruction of the ophthalmic veins by the increased intracranial pressure which is transmitted along the nerve sheath. In the early stages the margins of the optic discs are merely blurred and the retinal veins slightly engorged. As the condition progresses, the swelling of the nerve head increases and the physiological cup is obliterated. The veins become more engorged and retinal hæmorrhages may occur, and later the visual acuity deteriorates. Examination of the visual fields may be of great assistance in localizing a tumour, and various defects are found depending on the level in the optic nerves or tracts at which function is interrupted. The following two cases are examples of progressive blindness in which improvement did not occur after successful operative removal of the lesion, which was performed too late.

CASE V.—Miss L.S., aged eighteen years, complained of progressive loss of vision, and later she became ataxic. When I first examined her she could barely distinguish light from dark, and advanced secondary optic atrophy was present on both sides. A large cystic astrocytoma was removed from her cerebellum, and although she recovered completely in all other aspects, she did not regain any of her lost vision.

CASE VI.—Miss V.N., aged sixteen years, was completely blind when she was first referred to me, and she was also ataxic in her movements. She also had a large cystic astrocytoma of her cerebellum, which was removed at operation. All her symptoms disappeared except her loss of vision, and she is still totally blind.

Third, Fourth and Sixth Cranial Nerves.—The third, fourth and sixth cranial nerves are tested together, as they all control eye movement, while the third nerve also controls the size of the pupil and upper lid movement. Paralysis of the fourth or sixth nerve is of little localizing value, because the long course of these nerves subjects them to the influence of increased pressure irrespective of the site of the causative lesion. On the other. hand, interference with function of the third nerve is of vital importance. This nerve has three functions—it constricts the pupil, rotates the eyeball medially and elevates the upper lid, so that complete paralysis of the nerve would result in a dilated pupil that did not react to light, in external strabismus and in ptosis of the upper lid. The third nerve is exposed to pressure during its course from the midbrain to the cavernous sinus. This pressure may be exterted directly by a tumour or more frequently by the herniated anterior end of the hippocampal gyrus. Occasionally partial or complete third nerve palsy occurs in migraine. When all three nerves are involved, the lesion is usually in the region of the cavernous sinus as an aneurysm or other tumour. If one or more of these nerves is affected, one should always think of a cerebral tumour.

Fifth Cranial Nerve.—The trigeminal nerve is rarely affected in cerebral tumour, but when it is, the lesion is usually situated in the cerebello-pontine angle or near the cavernous sinus.

Seventh Cranial Nerve.—Lower facial movements are affected in lesions of the pyramidal tract, and facial paralysis may be part of a complete hemiplegia. The forehead is innervated from both cerebral hemispheres, consequently it is not greatly affected in lesions of one pyramidal tract. If the whole of one side of the face is paralysed, including the forehead, the lesion must be at or below the level of the facial nucleus. This could be the result of a pontine tumour, but it is usually a condition of facial or Bell's palsy.

Eighth Cranial Nerve.—Eighth nerve tumours are not uncommon, and are suggested by progressive nerve deafness, tinnitus and loss of balance. Labyrinth tests reveal a delayed or absent response. As the tumour grows, it compresses the pons, and the trigeminal and facial nerves may be affected.

Ninth, Tenth, Eleventh and Twelfth Cranial Nerves.—The ninth, tenth, eleventh and twelfth cranial nerves are rarely affected by intracranial expanding lesions, except those that involve the pons and medulla, in which case any surgical removal is usually not possible.

Motor System.

All movements should be examined for weakness or paralysis. Hemiplegia usually indicates a lesion in the opposite cerebral hemisphere, but it may occur on the same side as the lesion. In the latter case a large tumour pushes the mid-brain towards the opposite side and forces the opposite *crus cerebri* against the sharp non-yielding free edge of the *tentorium cerebelli*. In this manner the opposite pyramidal tract fibres are damaged above their point of decussation, an ipsilateral hemiplegia being produced. Although loss of muscle power may result from a variety of neurological lesions, an intracranial or intraspinal expanding lesion must always be kept in mind, especially when the signs are unilateral or segmental in distribution. An intraspinal tumour usually produces bilateral sensory or motor signs below its segmental level, and in the later stages bladder and bowel control may be affected. Sometimes, however, a small intraspinal tumour may be more selective and may affect only one or two spinal tracts. Muscle wasting and fibrillation suggest a lower motor neurone lesion which is usually degenerative in nature but may be due to a tumour. It is important to note the state of muscle tone in the extremities. This is usually of little value if the tone is equal on the two sides; but it is important if there is any difference. In pyramidal tract lesions, provided the reflex arc is preserved, the tone of the muscles below the lesion level is usually increased. In lesions in which the reflex arc is

involved, muscle tone is diminished. Diminution of tone is also found in lesions of the cerebellum and occasionally in lesions in which the motor cortex is involved.

Reflexes.

Alterations in deep reflexes are of great assistance in revealing the presence of a pyramidal tract lesion. In the majority of cases in which the reflex arc is preserved, the reflexes are exaggerated owing to loss of cortical control; but when the reflex arc is interrupted by the lesion the deep reflexes are diminished or absent. Any difference in a reflex response on the two sides is of far grater importance than when the reflexes are hyperactive or hypoactive, but equal. Usually differences in reflexes are fairly obvious, but sometimes the examiner must test a reflex many times to detect a minor irregularity. Reflexes may be roughly divided into two groups—deep and superficial. The main deep or tendon reflexes are the biceps, triceps, supinator, patellar, quadriceps (knee), and *tendo Achillis* (ankle). I have adopted numerical symbols to represent variation in reflex response, and *plus* or *minus* signs may also be used to indicate finer differences (see Table I).

TABLE I.

State of Reflex.	Right.	Left.
Absent	0	0
Diminished	1	1
Normal	2	2
Increased	3	3
Increased with temporary clonus	4	4
Increased with sustained clonus	5	5

Superficial or cutaneous reflexes are also valuable in revealing a pyramidal tract lesion when the reflex is diminished or absent. The more commonly known of these are the abdominal, cremasteric, plantar and grasp reflexes. The abdominal reflexes are really represented by three separate segments, but for practical purposes they can be subdivided into upper and lower reflexes, or more roughly stated as one unit on each side. The last-mentioned method is quite accurate for intracranial lesions. It must be remembered that abdominal reflexes are subject to a considerable amount of normal variation, as in patients with fat or flabby abdominal walls, so that little importance can be attached to abdominal reflexes that are equal whether they are hypoactive or hyperactive. The cremasteric reflex is elicited by stroking the inner side of the thigh, causing a contraction of the cremaster muscle which elevates the testicle on that side. The same comments apply to this as to the abdominal reflex.

The plantar or Babinski's reflex is the most important of the superficial reflexes with regard to pyramidal tract lesions. It should be tested by stroking the outer side of the sole, which produces a dorsiflexion of the great toe and fanning of the other toes in a pyramidal tract lesion, and plantar flexion of the toes in the normal subject. Do not stroke any part of the sole at random, because sometimes a dorsiflexor response may be obtained by stroking the inner side of the sole while a normal plantar flexor response follows stroking of the outer side of the sole. The plantar reflex may be checked by Oppenheim's reflex, in which firm moving pressure on the skin over the tibia causes dorsiflexion of the great toe. The grasp reflex is obtained by touching the palm of the patient's hand, especially between the thumb and forefinger, when the hand will grasp the object and the patient may be unable to let go voluntarily. This usually occurs in lesions involving the upper medial aspect of the opposite frontal lobe. It may, however, result from disturbance of frontal lobe function by tumours in other parts of the brain. Numerous other reflexes have been described, but those noted above are the most important.

Sensation.

Alteration in various sensations may afford an important clue to a localized lesion of the central nervous system. Pain, touch and temperature are the most important sensations and are tested by a moderately sharp pin, cotton wool and two test-tubes containing hot and cold water respectively. There are other forms of sensation which can be tested, such as tactile discrimination, vibration, postural sensibility and passive movement. These are refinements that may help towards localization; but in a routine examination testing of the sensations of pain, touch and temperature is usually sufficient to reveal any abnormality. Care should be taken in testing sensory loss in an hysterical patient. In such cases there is usually a circular upper level without any definite segmental distribution. If there is any doubt, the patient should be regarded as a tumour suspect and further tests should be carried out. In expanding lesions within the spinal canal, the sensory loss has a segmental distribution if the nerve roots alone are involved, and a segmental upper level with impairment below if the sensory tracts in the spinal cord are affected. Sensory loss from intracranial expanding lesions is not common unless a large area of the post-central cortex or sensory pathways is involved. Occasionally one finds hyperæsthesia or actual pain in an extremity due to a tumour involving the basal ganglia.

Coordination.

Tests are carried out to detect any evidence of incoordination on movement in one or other of the patient's extremities. In the upper extremity this may be done by the finger-nose-finger test, in which the patient alternately touches the tip of his own nose and the examiner's finger. The finger-to-finger test is carried out by the patient swinging his arms through a wide arc to bring the tips of his two index fingers together. Ability to perform rapidly alternating movements synchronously is tested by having the patient pronate and supinate his hands and forearms as quickly as possible or by having him pat the bed with both hands. Coordination of the lower extremities is tested by the heel-knee-tibia test in which the patient places one heel on the opposite knee and runs it downwards along the blade to the ankle. All these tests should be done first with the eyes open so that the patient can seen what he is doing, and then with the eyes closed. Evidence of incoordination usually indicates a lesion of the cerebellum or of certain of the cerebellar tracts. In such cases a true incoordination is present which shows little or no aggravation when the eyes are closed. In certain postcentral cortical lesions, in which loss of postural sensibility and of power of appreciation of passive movement is present, one may find a type of incoordination which is hardly noticeable when the patient's eyes are open, but which is pronounced when the eyes are closed. This is not true incoordination, as the muscles can coordinate well when the patient is able to see what he is doing, but the tests are not accurately performed when he is deprived of the aid of vision. Incoordination of an extremity usually indicates a cerebellar lesion on the same side, but occasionally it is found in the presence of a frontal lobe tumour of the opposite side.

Walking and Station.

Valuable information may be obtained by observing abormalities in the patient's gait and in his standing with his eyes open and closed. An ataxic gait may indicate a lesion in the cerebellum, in the labyrinth or occasionally in one or other frontal lobe. Such ataxia may be due to a degenerative lesion or to an expanding lesion. A spastic gait, especially if unilateral, is indicative of a pyramdal tract lesion which may be in the form of a tumour. Unsteadiness when standing with the heels and toes together is also suggestive of such a lesion. In this test one must be careful of the patient who is hysterical or who is malingering. In true ataxia a person may fall when his eyes are closed unless the examiner catches him, and he will make no effort to recover himself until it is too late. A patient who is hysterical or who is malingering will give a rather exaggerated exhibition of falling when his eyes are closed, but he will always see fit to recover himself when he reaches a certain angle, and if he does fall it is purely by accident.

Autonomic System.

The examiner should look for undue dryness, sweating, redness or pallor of the skin. One rarely finds evidence of

autonomic disturbance in tumours of the nervous system, except in the later stages when the extremities may be cold and clammy with excessive sweating.

Special Methods of Investigation.

Spinal, Cisternal and Ventricular Puncture.

A lumbar puncture should be performed in every case of suspected tumour. A fine 22-gauge needle should be used, as a larger needle may leave a small hole in the dura and arachnoid through which the cerebro-spinal fluid may escape, with subsequent reduction in pressure which may be dangerous. If the pressure is within normal limits, sufficient fluid should be withdrawn for the necessary laboratory tests. The normal findings in the cerebro-spinal fluid are as follows:

Pressure: 80 to 180 millimetres of water (horizontal).
Colour: Fluid is clear and colourless.
Cell content: 0 to 5 lymphocytes per millilitre.
Globulin content: 0.
Protein content: 5 to 45 milligrammes *per centum*.
Sugar content: 50 to 80 milligrammes *per centum*.
Chloride content: 720 to 750 milligrammes *per centum*.
Colloidal gold curve: 0000000000.

The fluid pressure when the patient is in the vertical position depends on the height of the patient, and in the normal subject the fluid reaches the level of the basal cistern. The protein content in the lumbar fluid is 15 to 45 milligrammes *per centum*, in the cisternal fluid it is 10 to 25 milligrammes *per centum*, and in the ventricular fluid it is 5·0 to 15 milligrammes *per centum*.

If the cerebro-spinal fluid pressure is high, only one or two cubic centimetres (including the fluid in the manometer) should be withdrawn very slowly. Rapid withdrawal of large quantities of fluid by the lumbar route, in cases of spinal or intracranial tumour, is extremely dangerous, and may well result in aggravation of the patient's symptoms and perhaps in rapid death. Cisternal or ventricular puncture to obtain fluid for testing is practically never indicated.

X-ray Examination.

Flat Plates.—Flat X-ray films of the skull or spine should always be taken in cases of a suspected tumour. In the spinal canal one may find widening of the canal or bone erosion, and in rare cases calcification in a spinal tumour will show up in the X-ray films. In viewing an X-ray film of the skull, one should look for evidence of erosion or hyperostosis of the bone and any abnormal formation of vascular channels. Calcification is frequently found in the pineal gland, which should lie in the mid-line, and a fine woolly type of calcification is also frequently seen in the chorioid plexus. This calcification is of no pathological significance, except when the shadow is displaced from its normal position. The pituitary fossa may be "ballooned" by a pituitary tumour, or the clinoid processes may be absorbed and enlargement of the pituitary fossa may be present owing to increased intracranial pressure.

Air Studies and X-ray Examination.—Ventricular air studies afford by far the most valuable information with regard to the presence and location of an intracranial expanding lesion. Cerebro-spinal fluid is replaced by air or oxygen, which is directed to the ventricular system, where it shows up as a dark shadow in the X-ray plates in contrast to the intracranial contents. If the cerebro-spinal fluid pressure is normal, then air may be injected through a lumbar puncture needle; but if an expanding lesion is suspected, only 20 to 25 cubic centimetres should be injected and the procedure should be stopped immediately on the slightest alteration in the patient's condition. If the intracranial pressure is high, the injection of air by the lumbar route is extremely dangerous and should never be attempted. In such cases the air should be injected directly into the lateral ventricles through a brain needle inserted through a burr hole in the skull. By the latter procedure, one is able to maintain a normal pressure much more accurately, and the burr hole acts as a safety valve to remove the air or reduce the pressure should the patient's condition deteriorate suddenly. If an expanding lesion is found, the surgeon should proceed immediately to remove it, as any delay caused by leaving the patient overnight after injecting air is very dangerous. If it is impossible to go ahead immediately with the major operation, or if operative removal is contraindicated, the air should always be removed through a brain needle after the X-ray pictures have been taken. This removal of air minimizes the risk, but does not completely eliminate it. In the films the configuration of the ventricular system is constant, with the exception of a good deal of individual variation in the occipital horns. Consequently one is able to recognize any variation in size, shape or position of the ventricular system as indicative of a lesion within the cranial cavity. If the pictures are satisfactory, it is possible to locate the exact position of an expanding or contracting lesion, or of obstruction at any point along the cerebro-spinal fluid pathways. Air has also been used as a contrast medium to localize lesions in the spinal canal. Unfortunately there are so many shadows of similar density in this region that it is usually difficult to make out the exact outline of the air. A positive result is valuable, but a negative result, which is much more frequent, is not sufficient to eliminate an expanding lesion.

Opaque Media and X-ray Examination.—Various opaque media have been used for the diagnosis and localization of intracranial and intraspinal expanding lesions. "Thorotrast" has been used to show up the ventricular system; but this procedure is extremely dangerous and I do not believe that it is ever justifiable. It has been shown that "Thorotrast" injected into the ventricles causes pronounced ependymitis and an inflammatory reaction in the subarachnoid space which may extend along the sheaths of the optic nerves. The most valuable use of this substance is in arteriography, especially for revealing the presence of an intracranial aneurysm. Arteriography has also been used to reveal the presence of a cerebral neoplasm by showing up the vascular pattern. This method was used by Monez of Madrid, but although I have seen several of his films in which the neoplasm was beautifully demonstrated, I do not think this procedure is comparable to ventricular air studies for efficiency or safety. Lipiodol has been of great value in localizing intraspinal expanding lesions. The main disadvantage of this substance is that it is never absorbed, and unless it is removed by operation, it becomes encysted within the spinal canal and remains there throughout the patient's life. Recently there have been reports in the literature of radio-opaque substances which are completely absorbed in one or two weeks. I have not yet used any of these, but if such a substance is perfected, it will completely replace the use of lipiodol within the spinal canal.

Electroencephalography.

In recent years the electroencephalogram has been used in some clinics to localize an intracranial expanding lesion. Unfortunately there are many technical difficulties in this procedure, and I have not yet had the courage to operate on electroencephalographic evidence alone without confirmation by ventricular air studies.

Biopsy.

In certain cases in which a lesion has been localized accurately, but in which the surgeon is uncertain of its pathological nature, a small piece of tissue may be sucked out through a biopsy needle and examined microscopically. In this manner the surgeon knows the type of lesion with which he is dealing, and is able to decide whether it is justifiable or not to attempt its removal. In other cases information may be obtained by inserting a brain needle into the suspected area. The experienced neurosurgeon is able to detect the difference in consistency when the needle passes through tumour tissue, and also in this manner he may encounter a cyst which would help him in his diagnosis.

Graduated Lumbar Manometric Test.

The graduated lumbar manometric test is used to detect the presence of a block in the cerebro-spinal fluid pathway, and can be performed with some degree of accuracy. Queckenstedt noted that pressure over the jugular veins caused a rapid rise of the spinal fluid column in a

manometer attached to a lumbar puncture needle. When this pressure was released, it was noted that the fluid fell rapidly to its original level. In the presence of a block the rise and fall of the fluid in the manometer are slowed to a degree depending on the completeness of the block. This, however, is a rather crude method, and merely indicates that a block exists somewhere between the cranium and the level of the lumbar puncture needle.

Some years ago William V. Cone and William Grant devised a method by which more accurate diagnosis could be made in cases of partial block and a rather rough localization could be assumed. In this procedure a gauge 18 lumbar puncture needle is inserted low down in the lumbar region and connected with a glass manometer. A sphygmomanometer cuff is wound round the patient's neck and held in place by a non-expansile bandage. The cuff is connected to the sphygmomanometer and inflated alternatively to pressures of 10, 20, 30 and 40 millimetres of mercury. The cuff pressure is maintained for ten seconds and then released. The manometer pressure reading is recorded five seconds and ten seconds after the neck cuff is inflated, and then every ten seconds after release of the cuff pressure until the spinal fluid returns to a steady level. In the normal subject the fluid pressure should reach its maximum within ten seconds and return to normal with five to ten seconds after release. Delay in the rise of the spinal fluid column, and more particularly in the fall after release, is indicative of partial block. If the block is complete, there is no movement at all of the spinal fluid column in the manometer. If there is evidence of a block by this method, the patient is then asked to give three consecutive coughs. If this causes a rapid rise and fall, it suggests that the block lies somewhere between the cranium and the thoracic level. If coughing produces a poor response, the patient is asked to strain as he would when at stool, and if this causes a rapid rise and fall in the spinal manometer it suggests that the block lies between the lumbar and thoracic regions. If there is a poor response on straining, it suggests that the lesion lies low down in the lumbar region. This procedure carries a certain degree of risk in the case of a complete spinal block, as it is likely to force the expanding lesion further downwards, and may increase the patient's symptoms even to the extent of a complete cord lesion at the level of the block. This procedure should never be carried out in the case of an intracranial expanding lesion, as it would be highly dangerous and would afford no important information. It is the practice of many to perform the ordinary manual Queckenstedt test when carrying out a lumbar puncture to ascertain the presence or absence of a block. I have little objection to this procedure in suspected spinal lesions, but I regard it as being extremely dangerous in intracranial lesions, and in the latter case the presence or absence of an obstruction to the cerebro-spinal pathway within the cranium could be more accurately ascertained by the less dangerous method of ventriculography.

Summary and Conclusions.

In this paper an attempt has been made to present, in an abbreviated form, the more important points to be considered in the early diagnosis of intracranial and intraspinal expanding lesions. It has been shown how essential it is to recognize these lesions at an early stage, for if they are permitted to extend beyond a certain point they must do so at the expense of the brain or spinal cord, and damage may be done which may be irreparable even after surgical removal of the tumour has been carried out. There are still many cases in which we are unable to carry out successful removal even when the condition is recognized early. It is doubtful if it will ever be possible to carry out a successful removal of malignant neoplasms involving the basal gangia, mid-brain, pons or medulla. Also it is very questionable if it is justifiable to remove cerebral metastatic tumours or rapidly growing gliomata. Excellent results, however, are obtained with the less malignant gliomata and with non-malignant tumours, provided that they have not progressed to the stage at which essential cerebral or spinal function is interfered with. Even at this stage one sometimes sees remarkable recoveries; but in such cases early recognition would mean a much smoother course for the patient and many fewer grey hairs for the neurosurgeon.

In conclusion, I should like to repeat one point. Every patient with symptoms referable to the central nervous system which become progressively worse should be regarded as a tumour suspect until proved otherwise, and should be subjected to a complete neurological investigation, including examination of the cerebro-spinal fluid and ventricular air studies.

STUDIES IN NICOTINIC ACID.

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BEFORE proceeding with an account of my work, I shall briefly reenlighten the reader's mind about the history and physiology of nicotinic acid. This digression is taken almost verbatim from the Nicholas vitamins manual (1943).

The realization in 1915 by Goldberger *et alii* that diet played a major role in the ætiology of pellagra led to the postulation by Goldberger and Tanner (1924) of a definite pellagra-preventive factor. In 1926 it was found that the thermostable portion of the vitamin *B* complex possessed pellagra-preventive properties. Then it was demonstrated by the experiments of Goldberger, Sebrell and others that black-tongue of dogs was analogous to human pellagra. Finally, Elvehjem and his collaborators (1937) isolated the nicotinic acid amide from liver concentrates and demonstrated that it cured dogs of black-tongue. The experiments by Spies (1938) and Harris (1937) on human pellagra showed that the pellagra-preventive factor had finally been discovered.

Although it has been suggested that nicotinic acid is not the only factor concerned in pellagra, present opinion is that although pellagra generally occurs in subjects with multiple deficiencies, deficiency of nicotinic acid or its active compounds is the only factor responsible for the characteristic symptoms of pellagra.

For about seventy-five years chemists have been familiar with nicotinic acid. Funk (1911), in his search for the antineuritic factor, isolated the acid, but failed to realize its nutritional significance. Chemically it is a pyridine β-carboxylic acid.

Although nicotinic acid is usually made commercially by the oxidation of nicotine, this reaction does not appear to be possible in the animal organism. Nicotinic acid is described in the Fourth Addendum to "The British Pharmacopœia" as a white crystalline powder which is odourless and has a feebly acid taste. Its melting point is 234° to 237° C. The acid and its solutions are stable under ordinary conditions and are unaffected even by strong oxidizing agents.

The chief dietary sources are meat and fish. Many cereals such as maize are very low in this factor, but wheat germ and unpolished rice form excellent sources. Yeast is also rich in nicotinic acid.

Nicotinic acid amide forms the prosthetic group of both coenzymes I and II. Coenzyme I consists of one molecule of nicotinamide linked to two molecules of phosphoric acid, one of adenine and two of pentose; whereas coenzyme II contains three molecules of phosphoric acid, but is otherwise chemically identical with coenzyme I. It is at present not clear whether the action of nicotinic acid is entirely due to its part in the production of the above-mentioned coenzymes, or whether its vitamin character is a function of some other properties.

Vasodilatation of the skin is produced by nicotinic acid and its salts, but not by the amide or diethylamide (nikethamide). It is interesting that the latter, better known as "Coramine", which possesses pellagra-preventive properties, has been used for many years as a cardio-respiratory stimulant.

Nicotinic acid and its amide are absorbed unchanged. Nicotinic acid is amidated in the organism after absorption in the blood stream. There are no special storage organs for nicotinic acid or its derivatives.

I. The Influence of Nicotinic Acid in Stimulating the Growth and Development of Primordial Follicles in Immature Virgin Guinea-Pigs.

Six virgin immature guinea-pigs were selected, and two were placed in each of three cages at the animal house attached to the Department of Physiology, Old Medical School, University of Sydney.

Method.

The experiment was carried out as follows.

On December 7, 1943, in the first cage, guinea-pig A was given an intramuscular injection of 25·0 milligrammes of nicotinic acid, and guinea-pig B was used as a control. In the second cage, guinea-pig A was given an intramuscular injection of 25·0 milligrammes of nicotinic acid, and guinea-pig B was used as a control. In the third cage, neither guinea-pig was treated.

On December 8, in the first cage, guinea-pig A was given 50·0 milligrammes of nicotinic acid orally; guinea-pig B was kept as a control. In the second cage, guinea-pig A was given 50·0 milligrammes of nicotinic acid orally, and guinea-pig B was used as a control. In the third cage, both guinea-pigs had their ovaries removed.

On December 9, in the first cage, guinea-pig A was given 50·0 milligrammes of nicotinic acid orally, and guinea-pig B was used as a control. In the second cage guinea-pig A was given 50·0 milligrammes of nicotinic acid orally, and guinea-pig B was used as a control. In the third cage, neither guinea-pig was treated.

On December 10, in the first cage, guinea-pig A was given 50·0 milligrammes of nicotinic acid orally and guinea-pig B was used as a control. In the second cage, guinea-pig A was given 50·0 milligrammes of nicotinic acid orally and guinea-pig B was used as a control. In the third cage, neither guinea-pig was treated.

On December 11, in the first cage, guinea-pig A was given 50·0 milligrammes of nicotinic acid orally and guinea-pig B was used as a control. In the second cage, guinea-pig A was given 50·0 milligrammes of nicotinic acid orally and guinea-pig B was used as a control. In the third cage, neither guinea-pig was treated.

On December 13, in the first cage, guinea-pig A was given 75·0 milligrammes of nicotinic acid orally and guinea-pig B was used as a control. In the second cage, guinea-pig A was given 75·0 milligrammes of nicotinic acid orally and guinea-pig B was used as a control. In the third cage, guinea-pigs A and B were each given 50·0 milligrammes of nicotinic acid orally.

On December 14, in the first cage, guinea-pig A was given 75·0 milligrammes of nicotinic acid orally, and guinea-pig B served as a control. In the second cage, guinea-pig A was given 75·0 milligrammes of nicotinic acid orally, and guinea-pig B served as a control. In the third cage, guinea-pigs A and B were each given 75·0 milligrammes of nicotinic acid orally.

On December 15, in the first cage, guinea-pig A was given 75·0 milligrammes of nicotinic acid orally, and guinea-pig B served as a control. In the second cage, guinea-pig A was given 75·0 milligrammes of nicotinic acid orally, and guinea-pig B served as a control. In the third cage, guinea-pigs A and B were each given 75·0 milligrammes of nicotinic acid orally.

On December 16, in the first cage, guinea-pig A was given 75·0 milligrammes of nicotinic acid orally, and guinea-pig B served as a control. In the second cage, guinea-pig A was given 75·0 milligrammes of nicotinic acid orally, and guinea-pig B served as a control. In the third cage, guinea-pigs A and B were each given 75·0 milligrammes of nicotinic acid orally.

On December 20, in the first cage, guinea-pig A was given 150·0 milligrammes of nicotinic acid orally, and guinea-pig B served as a control. In the second cage, guinea-pig A was given 150·0 milligrammes of nicotinic acid orally, and guinea-pig B served as a control. In the third cage, guinea-pigs A and B were each given 150·0 milligrammes of nicotinic acid orally.

On December 21, in the first cage, guinea-pig A was given 150 milligrammes of nicotinic acid orally, and guinea-pig B served as a control. In the second cage, guinea-pig A was given 150·0 milligrammes of nicotinic acid orally, and guinea-pig B served as a control. In the third cage, guinea-pigs A and B were each given 150·0 milligrammes of nicotinic acid orally.

On December 22, in the first cage, guinea-pig A was given 150 milligrammes of nicotinic acid orally, and guinea-pig B served as a control. In the second cage, guinea-pig A was given 150·0 milligrammes of nicotinic acid orally, and guinea-pig B served as a control. In the third cage, guinea-pigs A and B were each given 150·0 milligrammes of nicotinic acid orally.

On December 23, Guinea-pig A was given 150·0 milligrammes of nicotinic acid orally, and guinea-pig B served as a control. In the second cage, guinea-pig A was given 150 milligrammes of nicotinic acid orally, and guinea-pig B served as a control. In the third cage, guinea-pigs A and B were each given 150·0 milligrammes of nicotinic acid orally.

On December 24, all the animals were anæsthetized into oblivion. The following organs were placed in formalin for twenty-four hours, and then washed in and stored in 70% alcohol: (i) pituitary gland, (ii) ovary, (iii) Fallopian tubes, uterus, vagina, (iv) liver, (v) pancreas, (vi) adrenals.

Owing to difficulty in having sections of the organs made and stained, only the ovaries were examined microscopically. After being dried and weighed these were prepared in March, 1944, by Dr. Rushworth, pathologist to the Marrickville District Hospital.

Results.

Both ovaries of each animal were weighed together (sum) in milligrammes, and the weights were as follows: (i) first control 36·0 milligrammes, second control 37·0 milligrammes, average 36·5 milligrammes; (ii) first treated guinea-pig 45 milligrammes, second treated guinea-pig 44 milligrammes, average 44·5 milligrammes. There was thus an increase of five milligrammes in the weight of the ovaries in the treated animals, which represents an increase of 22% by weight in the treated animals.

The weights of the pituitary glands were as follows: (i) first control 7·6 milligrammes, second control 7·4 milligrammes, average 7·5 milligrammes; (ii) first treated guinea-pig 6·5 milligrammes, second treated guinea-pig 6·0 milligrammes, average 6·25 milligrammes; (iii) first ovariectomized guinea-pig 6·5 milligrammes, second ovariectomized guinea-pig 6·3 milligrammes, average 6·4 milligrammes. Thus there was a decrease in weight of 1·25 milligrammes in the pituitaries of the treated animals. This represents a decrease of 20% by weight in the pituitaries in the treated animals.

Conclusion.

In view of the fact that only four animals were used, the experiment as such is inconclusive; but from the results obtained the percentage increase in the weight of the ovaries and the percentage decrease in the weight of the pituitaries in the treated animals are almost in inverse proportion. This is interesting, in the light of the complex yet harmonious roles played by the gonadotrophic hormones of the anterior lobe of the pituitary and those elaborated by the Graafian follicle and the *corpus luteum* in the normal œstrous cycle.

This increase in weight in the treated ovaries is not due to an increase in the ovarian stroma, but to the rapid proliferation and ripening of many primordial follicles. The ovary was studded with an increased number of ripe ovarian follicles.

II. The Clinical Effects of Nicotinic Acid in Amenorrhœa, Hypomenorrhœa and Dysmenorrhœa.

Amenorrhœa.

Briefly, absence of cyclic menstruation may be physiological or pathological. The former type occurs before puberty, after the menopause, during pregnancy and generally during lactation. Ovulation does not occur before puberty, during pregnancy or following the menopause, but may occur during lactation, as is evidenced by the number of women who become pregnant during that period before menstrual bleeding has been reestablished. Pathological amenorrhœa may be primary or secondary. The former type is due to congenital defects or to abnormalities acquired during early childhood. The latter

type is due to abnormalities acquired after the menstrual cycle has been inaugurated.

Amenorrhœa may also be classified as primary and secondary.

Primary Amenorrhœa.

Amenorrhœa is regarded as primary when menstruation has never appeared during the menstrual span of the woman's life—that is, from the usual age of puberty to the age of the menopause. Two types of primary amenorrhœa are usually met with, (i) one in which amenorrhœa is associated with arrested physical development and an absence of secondary sexual characteristics, and (ii) one in which the somatic development is normal.

Primary amenorrhœa with arrested physical development and an absence of secondary sexual characteristics may be due to congenital defects of pituitary, thyreoid, suprarenal cortical or ovarian origin. It may result from endocrine disorder acquired during childhood or adolescence. Congenital amenorrhœa of pituitary origin is seen occasionally in Fröhlich's syndrome, in pituitary infantilism, and in certain types of tumours affecting the chromophobes as well as in lesions involving the hypothalamus. Congenital amenorrhœa of thyreoid origin is seen in cretins and in lesser manifestations of the hypothyreoid state. Amenorrhœa of suprarenal cortical origin is best exemplified by pseudohermaphroditism and virilism, resulting from a congenital tumour of the suprarenal medulla.

Primary amenorrhœa of ovarian origin may occur in congenital tumours (arrhenoblastoma) and in aplasia or other defects of the ovaries which cause them to be functionless—for example, atresia of the ovarian follicles, retention cysts of the ovary or fibroid infiltration and degeneration. The arrest in ovarian development may be either primary ovarian defect or secondary to anterior pituitary or to suprarenal cortical abnormality.

Primary amenorrhœa, with the exception of that due to primary ovarian defect, is associated with other congenital anomalies such as infantilism and rudimentary somatic development, aplasia of the external genitals and uterus, and the absence of other secondary sexual characteristics.

Amenorrhœa due to congenital ovarian defects is generally associated with pronounced somatic changes. Some of these patients may present masculine characteristics; this is particularly true in cases of arrhenoblastoma. In these patients there occur hypertrichosis and masculine bodily configurations and mannerisms. Similar changes are found in the presence of certain tumours of the suprarenal cortex. Other patients may present hypoplasia of the genitals, poorly developed secondary sex characteristics, and some change in stature, such as being too tall and thin, or too short and stout, or too short and thin. The skin is usually smooth, the fingers and extremities are long, and as a rule other hyperthymus characteristics are present. The pituitary sex hormone content in the blood is increased above normal and the œstrin level is diminished. Primary amenorrhœa of acquired origin with normal somatic development may be due to causes occurring at any time in the child's life from birth to just prior to puberty. Therefore somatic development need not be greatly affected. The amenorrhœa may be of non-endocrine origin, resulting from infectious diseases such as typhoid fever, scarlet fever, diphtheria or blood stream infections, or from local or general tuberculosis as well as from syphilis and other degenerative or inflammatory lesions. Amenorrhœa due to these conditions is usually temporary and may be considered as delayed menstruation. Occasionally it may be permanent, resulting from irreparable damage to the pituitary bodies or the ovaries. Permanent amenorrhœa of this type is generally of endocrine origin and of late development, and may be due to inflammatory lesions, cysts or syphilis, or to tumours of the pituitary, the adrenal cortex, the ovaries, the uterus or the Fallopian tubes. At times neither cause nor lesion is discoverable. Somatic changes may be absent, since here it is assumed that the lesions responsible for the amenorrhœa have developed too late to interfere with general bodily growth and development. Gigantism and acromegaly are often associated with this type of amenorrhœa.

Secondary Amenorrhœa.

By secondary amenorrhœa is meant the cessation of menstruation after it has been definitely established. The cause may be endocrine or non-endocrine. Secondary amenorrhœa of endocrine origin may be found in association with pituitary tumours or inflammation, or Simmonds's disease, and occasionally in exophthalmic goitre, in hypothyreoidism, in obesity and in diabetes.

Pathological lesions of the genital tract are responsible for most of the cases of secondary amenorrhœa. Among these lesions may be mentioned ovarian tumours, follicle cysts, retention cysts, and acute and chronic infections and fibrosis of the ovaries, the Fallopian tubes and the uterus.

The non-endocrine causes of amenorrhœa are many and are little understood. Psychic, nervous and emotional disturbances may cause temporary or permanent amenorrhœa. This is seen in the various types of psychoses and in profound emotionalism. Pseudocyesis may occur in those who fervently desire to become pregnant as well as in those who dread pregnancy. Amenorrhœa may also be found as the result of chronic infections, obesity, anæmia, leuchæmia, chlorosis and starvation.

The Relation of Amenorrhœa to Ovulation.

In the great majority of cases ovulation does not occur in the absence of menstruation. Occasionally, however, ovulation does occur in amenorrhœa. This is proved by the number of women who become pregnant, even though they have never menstruated.

The foregoing discussion on the various types and causes of amenorrhœa, for which I am indebted to S. A. Loewenberg's "Clinical Endocrinology", is essential for a clear understanding of the following clinical cases.

CASE I.—A single woman, aged twenty-four years, who had never menstruated, was short and plump, with broad shoulders and narrow hips and unusually smooth skin. There was no evidence of breast formation, or of pubic or axillary hair. In fact, she was completely devoid of secondary sex characteristics which signify functioning ovaries. It was evident she was suffering from primary amenorrhœa of ovarian origin. Her physician aptly described her secondary sexual development as being that of a child, aged ten years.

During January, February and March, 1942, she was subjected to a course of œstrone therapy. By such means two artificial "floodings" were induced, each occurring as an œstrone-withdrawal effect on the day after the last œstrone tablet had been taken. Treatment was then suspended. During the remainder of the year 1942 she gained seventeen pounds in weight. But, apart from the two artificial hæmorrhages (which were not true menstruation), she experienced no menstrual periods.

In May, 1943, for a chronic inflammatory lesion in the corners of her mouth she was ordered "Vibex" tablets with nicotinic acid (Parke, Davis and Company, Limited) containing 1·0 milligramme of thiamin and 25 milligrammes of nicotinic acid. In June she menstruated, the flow being normal in duration, quantity and quality. The mouth lesion cleared up and I induced her to continue with the nicotinic acid tablets. She did not menstruate in July, but still taking tablets, she menstruated again in August. She missed her period in September, but responded again in October and in November. During these seven months there was a rapid development of the secondary sexual characteristics. Treatment was then suspended, and she has menstruated regularly since and has since married. Her dose was one tablet three times a day, and only once did she exhibit signs of intolerance—peripheral vasodilatation, tingling in the extremities and profound irritability, which rapidly passed off within an hour or two. During this treatment she lost weight rapidly (approximately eighteen pounds in four months).

CASE II.—A single girl, aged nineteen years, had primary amenorrhœa of ovarian type. The secondary sexual characteristics were grossly underdeveloped. She was given 25 milligrammes of nicotinic acid three times a day for two months. There was no effect. The dose was increased to fifty milligrammes three times a day, and there were still

no signs of menstruation; breast changes and the usual accompanying phenomena of development became evident. Within six months from the beginning of treatment she had her first menstrual period. For the next six months the intervals between the periods were seven weeks and six weeks, and now the menstrual periods are regular in time and duration and the flow is of normal quantity. Over the twelve months the patient lost twelve pounds in weight.

CASE III.—A married woman, aged thirty-two years, on vaginal examination was found to have a small, fibromuscular uterus. There was no change after six months' therapy.

Hypomenorrhœa.

Hypomenorrhœa is the term generally applied to conditions in which menstruation occurs regularly, but clinically the flow is of insufficient quantity. The menstrual flow may be represented by a few spots occurring daily for one, two or three days, or the quantity of blood lost may be sufficient to stain two or three diapers a day for a few days.

The direct cause of scanty menstruation is insufficient endometrial change, resulting from either insufficient ovarian hormone stimulation or local uterine abnormality due to defective ovaries, hypopituitarism or hypothyreoidism.

The production of an insufficient amount of ovarian hormone may be due to local or congenital disease of the ovaries, or to the more common cause, hypofunction of the anterior pituitary body, in which the quantity of prolan produced is insufficient for proper stimulation of ovaries and uterus.

In hypomenorrhœa of all types the œstrin content of the blood and urine is below normal.

Hypomenorrhœa due to uterine abnormality may be acquired subsequent to the existence of normal menstruation, for example, by frequent curettage, chemical cauterization, or radium implantation, which have a tendency to destroy much of the basal layer of the endometrium so that it becomes incapable of responding to ovarian stimulation.

CASE IV.—A married woman, aged twenty-seven years, had had a scanty but regular menstrual flow since puberty, which became established at thirteen years of age. Before 1938 her weight was seven stone four pounds; before she commenced treatment in July, 1944, it was ten stone nine pounds, and her height was five feet one inch. She is thus short and plump, with well-developed secondary sex characteristics.

On July 19, 1944, she commenced treatment, taking one tablet of "Vibex" with nicotinic acid three times a day until she menstruated on August 3. There was no difference in the duration, which is always less than twenty-four hours, nor in the quantity of blood lost, which is scanty. She was thus taking the tablets during the *corpus luteum* phase of the menstrual cycle, and there was no appreciable difference. No tablets were taken between August 3 and 31, when she menstruated again. This time the menstrual period lasted for forty-eight hours and the quantity of blood lost was approximately twice as much as previously. On September 2 she recommenced taking the tablets and continued until September 14, when they were stopped, as menstruation commenced. This period was of a most profuse type; it lasted until October 12, and simulated the condition of *metropathia hæmorrhagica*, there being a proliferative phase but no secretory phase. Large clots were voided, but there was no dysmenorrhœa. During this stage she was ordered "Polyhæmen" tablets, and she lost nine pounds in weight in twelve days. She has not taken any nicotinic acid tablets since September 14, 1944, and her menstrual periods are still within normal range with regard to duration and to quantity and quality of the menstrual flow.

CASE V.—A nurse, aged twenty years, was five feet two inches in height and ten stone seven pounds in weight. The menstrual flow was scanty, lasting from eight to twenty-four hours. After she had taken nicotinic acid tablets, fifty milligrammes three times a day for one month, there was no appreciable change in the corresponding monthly period. Treatment was continued for another twenty-eight days. The flow at the end of this month lasted five days, and for the last five menstrual periods it has fluctuated between four and six days. There was a loss of twenty pounds in weight in three months.

CASE VI.—Mrs. H.G.K., of Tasmania, was five feet one inch in height and eleven stone eight pounds in weight. The menstrual flow lasted eight to twenty hours. She had no children, but was desirous of pregnancy. Over a period of three months she received weekly injection of theelin in oil. At the end of the third month menstruation occurred and lasted for two and a half days. However, her next three menstrual periods were as usual. She was then given fifty milligrammes of nicotinic acid three times a day, commencing on the first day of her menstrual period. After thirty days the patient experienced a menstrual period lasting for seven days. The following five menstrual periods lasted between five and seven days. The patient is still sterile.

CASE VII.—Mrs. M.S., of New South Wales, was ten stone seven pounds in weight and five feet two inches in height. Her menstrual periods usually lasted from twelve to thirty-six hours, and were regular in time. She had been married for four years and had no children, although she wanted them. Within three months after the usual nicotinic acid therapy she had a monthly menstrual period lasting five days. Treatment was then suspended. Over the past year the menstrual periods have lasted from five to six days and are regular in time and in the quantity and quality of the flow. She became pregnant.

CASE VIII.—Mrs. Q., of Tasmania, aged forty years, was sterile. Normally the menstrual periods lasted from four to forty-eight hours. After two months' stimulation with nicotinic acid a flow lasting three days was induced, and for the past five months the flow has lasted between three and five days. She is still sterile.

CASE IX.—Mrs. R.H., of Tasmania, was five feet two inches in height and eight stone four pounds in weight. She had been married for two years, without children, but was hoping to become pregnant. The menstrual periods usually lasted approximately two days. After treatment with nicotinic acid for sixty days the menstrual periods began to last from three to five days, and she became pregnant.

Three other patients with hypomenorrhœa were also successfully treated. Two of these three received one milligramme of stilbœstrol three times a day for fourteen days from the commencement of the flow, together with nicotinic acid, fifty milligrammes three times a day, from the beginning of one period to the beginning of the following period. There was a rapid response by these two patients compared to the other patient, who received only nicotinic acid for the same period.

In a further two cases there was no change whatsoever after three months' treatment. In the case of married women, pelvic examinations were conducted to exclude pathological lesions in the pelvic organs. This examination was not made in the case of single women.

Dysmenorrhœa.

Dysmenorrhœa may be primary when it is not dependent upon a definite pelvic lesion, and secondary when it is caused by distinct pelvic abnormality. The pain may precede the beginning of the menstrual flow of each cycle by a few hours, or by one or two days, and it may continue with the flow from a few hours to one or two days until free bleeding is established. In rare cases the pain may continue during the entire period.

The cause of primary dysmenorrhœa is not definitely known. There seem to be several factors responsible for this anomaly.

Nervous causes, including psychic disturbances and instability of the autonomic nervous system, may be operative. Either there exists a common cause for both the dysmenorrhœa and the autonomic nervous system disturbances, or the one causes the other. The fact that dysmenorrhœa is more prevalent among neurotic, highly strung and emotional women indicates that psychogenic factors or the adrenal medulla play a part.

Hypoplasia or obstruction of the uterus may be present; the cervical canal and possibly also the Fallopian tubes may cause pain when these structures are incapable of transmitting freely the discharging blood and the frequently accompanying solid particles.

Endocrine disturbances causing spasticity are responsible for much dysmenorrhœa. The pain occurs usually on the first day of the flow and is spasmodic or colicky in nature. The nature of the pain would suggest a dis-

ordered and spasmodic contraction of the uterine muscle. While the uterine muscle is under the influence of œstrin, its motility is increased and it is more sensitive to pitocin. The *corpus luteum* hormone has a reverse effect and is an inhibitor of uterine contractions. In the latter half of the menstrual cycle, the luteal phase is superimposed upon the œstrus phase, and the action of the *corpus luteum* becomes more prominent until about four days before the menstrual flow commences; when the gland begins to retrogress. This withdrawal of the supply of progesterone allows unchecked the action of the œstrone, the content of which in the blood has been increasing steadily during the menstrual cycle and has reached its maximum a week before menstruation. Thus the motility of the uterine muscle is greatest on the first day of the flow and for one or two days beforehand.

Disordered contraction of the uterine musculature may, therefore, result from an imbalance of the ovarian hormones, which may be quantitative or chronological in nature. To argue more from theory than from fact, it might be supposed that the over-production of œstrone is an obvious cause of excessive uterine contractions and so of pain; but in the one condition of *metropathia hæmorrhagica* in which this is known to occur, painful menstruation is absent. On the other hand, the over-production of progesterone would result in an excessive development of the premenstrual decidua. The endometrium which is cast off would therefore be more compact and in consequence be shed in the form of portions of relatively tough tissue. Whereas in a large number of women the expulsion of such shreds of tissue is undoubtedly accompanied by severe uterine colic, cases occur in which whole casts of the endometrium are passed without undue pain, and in addition severe colic occurs without the passage of either clots of blood or shreds of endometrium.

Fifteen patients were treated; only three cases will be described in detail.

CASE X.—A woman, aged thirty-one years, had been married for ten years and suffered from painful menstruation. The pain was of a colicky nature and was referred to the sacrum and the umbilicus and down the inner side of the thighs. She was engaged in aircraft production, and was always compelled to stay home for at least two days during each menstrual period. During September and October, 1943, she was taking one tablet of "Vibex" with nicotinic acid three times a day, and the succeeding menstrual periods were of such a nature as not to compel her to absent herself from her work.

CASE XI.—A single girl, aged twenty-five years, had suffered from painful menstrual periods since puberty. Her menstruation was peculiar, in that within an hour of commencing the flow stopped and recommenced in about six hours, when large dark-coloured clots were voided. This was the painful stage, and lasted approximately ten to fifteen hours. The pain came and went in spasms during that time. From then onwards there was no pain. In the interim between September 2 and 16, 1944, she took one tablet of "Vibex" with nicotinic acid three times a day. Menstruation commenced on September 26. As previously, it started, stopped and restarted; but the clots were not dark and the pain lasted for only one and a half hours. She took the tablets again from October 1 to 19 and menstruated again on October 27. This time the pain lasted for one hour, and the starting, stopping and restarting mechanism was lost. Since then she has not complained of pain at the time of her menstrual periods.

CASE XII.—Miss Y.L., of Tasmania, aged seventeen years, complained of severe colicky pain in the suprapubic area and down the inner sides of both legs, associated with headache, loss of appetite, extreme irritability and occasionally vomiting persisting from twenty-four hours to forty-eight hours before the established onset of the flow. She was admitted to hospital for curettage in September, 1945. She was discharged on her admission and received nicotinic acid therapy combined with œstrone (to be described later). The October menstrual period was characterized by loss of distressing constitutional disturbances, and the pain, which was still acute, lasted for only two hours. The combined treatment was continued for one more month, and the November, December and January menstrual periods caused the patient no pain or accompanying distressing symptoms. There was a loss of ten pounds in weight in four months.

Combination of Œstrone and Nicotinic Acid Therapy in Dysmenorrhœa.

Of the fifteen patients selected, (i) five received only œstrone (one milligramme three times a day) from the first day of the flow for fourteen days; four noticed no effect over three months; (ii) five received only nicotinic acid (fifty milligrammes three times a day) from the first day of the flow for sixty days; there was little or no effect at the end of the first month and a better response at the end of the second month, and results were good from the third month onwards; (iii) five received combined œstrone and nicotinic acid treatment for sixty days; in these cases the response was immediate.

From the above cases it is apparent that whilst œstrone has a dubious effect and nicotinic acid alone has a delayed effect, the combination of the two in all cases produced a positive result in a shorter time from the beginning of treatment.

Whenever possible, pelvic examinations were made to exclude any pathological condition; but if the patient was virginal, this was not done.

CONCLUSION.

From the experiments on the guinea-pigs and from the clinical studies, it would appear that the ovaries respond to the influence of nicotinic acid. That this response occurs only in cases in which the ovary is not functioning normally, is evidenced by the fact that there is no appreciable difference in the duration, quantity or quality of the menstrual flow in women whose menstrual flow is normal in duration, quantity and quality, and who have received nicotinic acid therapy.

When the ovary is under-functioning, then the effect of nicotinic acid is most pronounced; this has been demonstrated in the case of primary amenorrhœa due to ovarian defect, and in the case of hypomenorrhœa. Whether this influence is directly upon the epithelial elements of the ovary, and specifically stimulates their growth and development, or whether it simulates the properties of a hormone and stimulates the immature or under-functioning primordial follicles through the anterior lobe of the pituitary gland, or whether its influence is through the autonomic nervous system, are questions I cannot answer.

Two points in particular are to be noted: (i) that a rapid loss of weight was experienced by the obese subjects whilst they were receiving nicotinic acid; (ii) that when œstrone and nicotinic acid are combined their function is enhanced. This phenomenon occurs also with parathormone and vitamin *D* in their action on calcium metabolism, and provides an interesting link between the properties of hormones and vitamins.

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ACCEPTABLE WORDS: QUOTATIONS WITH A MEDICAL BEARING.

By J. B. CLELAND,

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IN Ecclesiastes the preacher sought to find out acceptable words. And acceptable words are ever a pleasure to read, whether they are Shakespeare's linked sweetness, or the beautiful phraseology of the Authorized Version of the

Bible, or the gems that are to be found scattered through the writings of the masters of our language. Amongst these are not a few with a definitely medical bearing, and even in works on purely medical subjects acceptable words in harmonious association are not unknown. As these have delighted me from time to time and I turn again to them with renewed pleasure, it seemed worth while to bring together random notes made over many years, so that others may enjoy them as well as myself.

The Hippocratic Oath.

"I swear by Apollo the physician, and Æsculapius, and Health, and All-heal, and all the gods and goddesses, that, according to my ability and judgment, I will keep this Oath and this stipulation—to reckon him who taught me this Art equally dear to me as my parents, to share my substance with him, and relieve his necessities if required; to look upon his offspring in the same footing as my own brothers, and to teach them this Art, if they shall wish to learn it, without fee or stipulation; and that by precept, lecture, and every other mode of instruction, I will impart a knowledge of the Art to my own sons, and those of my teachers, and to disciples bound by a stipulation and oath according to the law of medicine, but to none others. I will follow that system of regimen which, according to my ability and judgement, I consider for the benefit of my patients, and abstain from whatever is deleterious and mischievous. I will give no deadly medicine to anyone if asked, nor suggest any such counsel; and in like manner I will not give to a woman a pessary to produce abortion. With purity and with holiness I will pass my life and practise my Art. I will not cut persons labouring under the stone, but will leave this to be done by men who are practitioners of this work. Into whatever houses I enter, I will go into them for the benefit of the sick, and will abstain from every voluntary act of mischief and corruption; and, further, from the seduction of females or males, of freemen and slaves. Whatever, in connection with my professional practice or not in connection with it, I see or hear, in the life of men, which ought not be spoken of abroad, I will not divulge, as reckoning that all such should be kept secret. While I continue to keep this Oath unviolated, may it be granted to me to enjoy life and the practice of the Art, respected by all men, in all times! But should I trespass and violate this Oath, may the reverse be my lot!"

—Francis Adam's translation.

Honour the Physician.

"Honour a physician with the honour due unto him for the uses which ye may have of him: for the Lord hath created him.

"For of the most High cometh healing, and he shall receive honour of the king.

"The skill of the physician shall lift up his head: and in the sight of great men he shall be in admiration.

"The Lord hath created medicines out of the earth; and he that is wise will not abhor them."

—Ecclesiasticus, Chapter XXXVIII, Verses 1 to 4.

"There are men and classes of men that stand above the common herd: the soldier, the sailor and the shepherd not unfrequently; the artist rarely; rarelier still, the clergyman; the physician almost as a rule. He is the flower (such as it is) of our civilization; and when that stage of man is done with, and only remembered to be marvelled at in history, he will be thought to have shared as little as any in the defects of the period, and most notably exhibited the virtues of the race. Generosity he has, such as is possible to those who practise an art, never to those who drive a trade; discretion, tested by a hundred secrets; tact, tried in a thousand embarrassments; and what are more important, Heraclean cheerfulness and courage. So it is that he brings air and cheer into the sickroom, and often enough, though not so often as he wishes, brings healing."

—Robert Louis Stevenson: dedication to "Poems".

"The medical profession occupies in the body social an unique position, and one prepotent of great good to the community at large. In the houses of the great, in the hovels of the poor, amongst the learned and the illiterate, the mentally sound, the morally degenerate and unfit, the doctor daily makes his round. All sides of life he sees, the many minor tragedies, grave crises, little comedies, unfathomable affections, unlooked-for kindliness of heart, and callous selfishness. All sorts and conditions of men it is his daily duty to study for guidance in his administration of the sick. When illness or trouble are present in the house, the outside mask of worldly life is discarded, and the true self stands revealed. The medical man, even beyond the clergyman, sees into the heart of the people, and knows and appreciates their desires. Moreover, he is skilled in weighing facts, and careful in drawing conclusions, he is accurate in summing-up, and broad-minded in the ways of the world. As a member of the most liberal of the professions, he sees what others would fail to grasp, and time and again his advice is sought by a friend, in the affairs of the world, not related to his work."

—"Medical Men and Social Problems", *The Australasian Medical Gazette*, June 20, 1911, page 331.

"A Physician in a great city seems to be the mere plaything of Fortune; his degree of reputation is for the most part casual; they that employ him know not his excellence; they that reject him know not his deficience."

—Samuel Johnson, quoted in *Nature*, August 26, 1920, page 812.

A Doctour of Phisike.

"With us ther was a DOCTOUR OF PHISIKE,
In all this world ne was ther non him like
To speke of phisike, and of surgerie:
For he was grounded in astronomie.

. . . . . .

He knew the cause of every maladie,
Were it of cold, or hote, or moist, or drie,
And wher engendred, and of what humour,
He was a veray parfite practisour."

—Geoffrey Chaucer, "The Canterbury Tales" ("The Prologue").

Let Us Praise Famous Men.

"Let us now praise famous men, and our fathers that begat us.

"The Lord hath wrought great glory by them through his great power from the beginning.

"Such as did bear rule in their kingdoms, men renowned for their power, giving counsel by their understanding, and declaring prophecies:

"Leaders of the people by their counsels, and by their knowledge of learning meet for the people, wise and eloquent in their instructions:

"Rich men furnished with ability, living peaceably in their habitations:

"All these were honoured in their generations, and were the glory of their times."

—Ecclesiasticus, Chapter XLIV, Verses 1 to 4, 6 and 7.

Bidding Prayer.

The following is the Bidding Prayer delivered by Professor J. L. Myres at the Commemorative Service at Liverpool Cathedral of the British Association for the Advancement of Science on Sunday, September 20, 1931. After each prayer the response of the Dean was "Bless ye the Lord", and of the congregation "Praise him and magnify him for ever". (*Nature*, October 3, 1931, page 573.)

"Ye shall remember those who in all times and in all places have devoted their gifts of intellect and imagination to interpret the laws of thought, the place of man in the universe, and the nature of reality;

"Such as were Aristotle, Da Vinci, Bacon, Descartes, and Kant.

"Ye shall remember all who have explored the properties of numbers, and the mysteries of time and space;

"Such as were Pythagoras, Archimedes, Newton, Leibnitz, Gauss, and Poincaré.

"Ye shall remember all who have determined the courses of the stars, the place among them of sun, moon, and this earth of ours, and have given to all those, whose business is in the great deep, sure guidance to the haven where they would be;

"Such as were Ptolemy, Copernicus, Kepler, Tycho Brahe, Holley, Herschel, and Huggins.

"Ye shall remember all whose profound vision and infinite patience have revealed the ever-changing uniformities of the great forces of Nature; and made light and sound, heat and cold, lightning, wind and flood subservient to the purposes of man;

"Such as were Galileo, Gilbert, Watt, Faraday, Joule, Clerk Maxwell, Rayleigh, Hertz and Parsons.

"Ye shall remember all who, not sparing life or fortune, set forth to find and win new homes for the multitude of our folk, to build the waste places of the earth, so that the desert should rejoice and blossom, and the men who stood far off might see a great light; for all travellers and explorers, and for those who were moved by great thought to send them forth, and to set down and make known their discoveries;

"Such as were Marco Polo, Prince Henry the Navigator, Christopher Columbus, Banks, Cook, Humboldt, Franklin, Livingstone, Nansen and Scott.

"Ye shall remember all who have set in order the lineage of all living things, animals and plants, observed their habits and haunts, their struggles and survivals throughout the long lapse of time, the wonderful variety, infinite beauty, and subtle adaptation of each to its proper life; their coming to birth and passing away; who have distinguished among them the friends and foes of man, and sought to diversify by human skill the manifold works of creation.

"Such as were Hippocrates, Galen, Linnæus, Cuvier, Lamarck, Darwin, Hooker, Huxley, and Mendel.

"Ye shall remember all who have applied the principles of the several sciences to the tillage of the soil, the avoidance of famine and pestilence, the breeding and sustenance of flocks and herds, and the abundant provision of our daily bread;

"Such as were Jethro Tull, Daubeny, Liebig, Lawes and Theiler.

"Ye shall remember all who, by their intimate study of the functions of life, have made plain the mysteries of many diseases and abated their ravages; and brought knowledge of our bodily frame to the better study of the mind in sickness and in health;

"Such as were Vesalius, Harvey, Hunter, Claude Bernard, Johannes Müller, Pasteur, and Helmholtz.

"Ye shall remember all whose contemplation of the divers races of mankind, the manner of their lives, the ordering of their societies, their customs and beliefs, and their manifold dealings each with his neighbour, for the enjoyment of Nature's gifts and the fruits of reason and toil, to the increase of the wealth of nations, have contributed to mutual understanding among the peoples and peace on earth among men of good will;

"Such as were Bodin, Locke, Montesquieu, Adam Smith, Quételet, Galton and Tyler."

Religio Medici.

The following excerpts are taken from "Religio Medici", by Sir Thomas Browne.

"Thus we are men, and we know not how; there is something in us that can be without us, and will be after us, though it is strange that it hath no history what it was before us, nor cannot tell how it entered in us." (Part I, Section 36.)

Of meeting death:

"This makes me naturally love a soldier, and honour those tattered and contemptible regiments, that will die at the command of a sergeant." (Section 38.)

Nature: "That universal and publick manuscript, that lies expansed unto the eyes of all." (Section 16.)

"I feel not in me those sordid and unchristian desires of my profession; I do not secretly implore and wish for plagues, rejoice at famines, revolve ephemerides and almanacks in expectation of malignant aspects, fatal conjunctions, and eclipses. I rejoice not at unwholesome springs nor unseasonable winters: my prayer goes with the husbandman's; I desire everything in its proper season, that neither men nor the times be out of temper. Let me be sick myself, if sometimes the malady of my patient be not a disease unto me. I desire rather to cure his infirmities than my own necessities. Where I do him no good, methinks it is scarce honest gain, though I confess 'tis but the worthy salary of our well intended endeavours. I am not only ashamed but heartily sorry, that, besides death, there are diseases incurable; yet not for my own sake or that they be beyond my art, but for the general cause and sake of humanity, whose common cause I apprehend as mine own. And, to speak more generally, those three noble professions which all civil commonwealths do honour, are raised upon the fall of Adam, and are not any way exempt from their infirmities. There are not only diseases incurable in physick, but cases indissolvable in law, vices incorrigible in divinity." (Part II, Section 9.)

"Now for my life, it is a miracle of thirty years, which to relate, were not a history, but a piece of poetry, and would sound to common ears like a fable. For the world, I count it not an inn, but an hospital; and a place not to live, but to die in." (Part II, Section 11.)

The Infancy of Saint Augustine.

"Thus there received me the comforts of woman's milk . . . For then I knew but to suck; to repose in what pleased, and cry at what offended my flesh; nothing more.

"Afterwards I began to smile; first in sleep, then waking: for so it was told me of myself, and I believed it; for we see the like in other infants, though of myself I remember it not. Thus, little by little, I became conscious where I was; and to have a wish to express my wishes to those who could content them, and I could not; for the wishes were within me, and they without; nor could they by any sense of theirs enter within my spirit. So I flung about at random limbs and voice, making the few signs I could, and such as I could, like, though in truth very little like, what I wished. And when I was not presently obeyed (my wishes being hurtful or unintelligible), then I was indignant with my elders for not submitting to me, with those owing me no service, for not serving me; and avenged myself on them by tears. Such have I learnt infants to be from observing them; and, that I was myself such, they, all unconscious, have shewn me better than my nurses who knew it."

—"Confessions of Saint Augustine", Book I, paragraphs 7 and 8.

Sleep.

"And, more to lulle him in his slumber soft,
A trickling streame from high rock tumbling downe,
And ever-drizling raine upon the loft,
Mixt with a murmuring winde, much like the sowne
Of swarming bees, did caste him in a swowne.
No other noyse, nor peoples troublous cryes,
As still are wont t' annoy the walled towne,
Might there be heard: but carelesse Quiet lyes,
Wrapt in eternall silence farre from enimyes."

—Edmund Spenser: "The Faerie Queene", Book I, Canto 1, line 41.

"Now blessings light on him that first invented this same sleep; it covers a man all over, thoughts and all, like a cloak; it is meat for the hungry, drink for the thirsty, heat for the cold, and cold for the hot. It is the current coin that purchases all the pleasures of the world cheap; and it is the balance that sets the king and the shepherd, the fool and the wise man." —Cervantes.

Right Judgement and Clinical Instinct.

"The one talent which is most worth all other talents put together in all human affairs is the talent of judging right upon imperfect materials, the talent if you please of guessing right. It is a talent which no rules will ever teach, and which even experience does not always give. It often coexists with a good deal of slowness and dulness, and with a very slight power of expression. All that can

be said about it is, that to see things as they are, without exaggeration or passion, is essential to it; but how can we see things as they are? Simply by opening our eyes and looking with whatever power we have. All really important matters are decided, not by a process of argument worked out from adequate premisses to a necessary conclusion, but by making a wise choice between several possible views."

—Stephen's "Liberty", *et cetera*, page 332; quoted by R. M. Hutchison, *British Medical Journal*, March 3, 1928, page 335, who adds the following:

"What is sometimes called 'clinical instinct' is, in truth, simply a power of rapid instinctive judgement, and it may be lacking in men of high intellectual ability and present to a marked degree in those who are in other respects mentally their inferiors. It seems to be much the same as 'common sense' and closely allied to a sense of humour, which is the same thing as a sense of proportion. Those who lack it are apt, in making a diagnosis, to fail to see the wood for the trees."

The Valley of Dry Bones.

"The hand of the Lord was upon me, and carried me out in the Spirit of the Lord, and set me down in the midst of the valley which was full of bones.

"And caused me to pass by them round about: and, behold, there were very many in the open valley; and, lo, they were very dry.

"And he said unto me, Son of man, can these bones live? And I answered, O Lord God, thou knowest.

"Again he said unto me, Prophesy upon these bones, and say unto them, O ye dry bones, hear the word of the Lord.

"Thus saith the Lord God unto these bones, Behold, I will cause breath to enter into you, and ye shall live:

"And I will lay sinews upon you, and will bring up flesh upon you, and cover you with skin, and put breath in you, and ye shall live; and ye shall know that I am the Lord.

"So I prophesied as I was commanded: and as I prophesied there was a noise, and, behold, a shaking, and the bones came together, bone to his bone.

"And when I beheld, lo, the sinews and the flesh came up upon them, and the skin covered them above; but there was no breath in them.

"Then said he unto me, Prophesy unto the wind, prophesy, son of man, and say to the wind, Thus saith the Lord God, Come from the four winds, O breath, and breathe upon these slain, that they may live.

"So I prophesied as he commanded me, and the breath came into them, and they lived, and stood up upon their feet, an exceeding great army."

—Ezekiel, Chapter XXXVII, Verses 1 to 10.

The Anatomist's Hymn.

"Not in the world of light alone,
Where God has built His blazing throne,
Nor yet alone in earth below,
With belted seas that come and go,
And endless isles of sunlit green,
Is all thy Maker's glory seen:
Look in upon thy wondrous frame,—
Eternal wisdom still the same!

"The smooth, soft air, with pulse-like waves,
Flows murmuring through its hidden caves,
Whose streams of brightening purple rush
Fired with a new and livelier blush,
While all their burden of decay
The ebbing current steals away,
And red with Nature's flame they start
From the warm fountains of the heart.

"No rest that throbbing slave may ask,
For ever quivering o'er his task,
While far and wide a crimson jet
Leaps forth to fill the woven net
Which in unnumbered crossing tides
The flood of burning life divides,
Then kindling each decaying part
Creeps back to find the throbbing heart.

"Then mark the cloven sphere that holds
All thought in its mysterious folds,
That feels sensation's faintest thrill,
And flashes forth the sovereign will:
Think on the stormy world that dwells
Locked in its dim and clustering cells!
The lightning gleams of power it sheds
Along its hollow glassy threads."

—Oliver Wendell Holmes: "The Autocrat of the Breakfast-Table".

Chlorosis.

". . . daffodils,
That come before the swallow dares, and take
The winds of March with beauty; violets dim,
But sweeter than the lids of Juno's eyes
Or Cytherea's breath; pale primroses,
That die unmarried ere they can behold
Bright Phœbus in his strength—a malady
Most incident to maids; bold oxlips, and
The crown-imperial; lilies of all kinds . . ."

—Shakespeare: *The Winter's Tale*, Act iv, Scene 3.

[Buckwill in "Shakespeare's Medical Knowledge", page 13, considers that this complaint was "consumption".]

". . . She never told her love,
But let concealment, like a worm i' the bud,
Feed on her damask cheek; she pined in thought;
And, with a green and yellow melancholy,
She sat like patience on a monument,
Smiling at grief."

—Shakespeare: *Twelfth Night*, Act ii, Scene 4.

[Buckwill, at page 122, gives other references to chlorosis.]

Infection.

"This royal throne of kings, this scepter'd isle,
This earth of majesty, this seat of Mars,
This other Eden, demi-paradise;
This fortress built by Nature for herself
Against infection and the hand of war;
This happy breed of men, this little world,
This precious stone set in the silver sea,
. . . . . .
This blessed plot, this earth, this realm, this England."

—Shakespeare: *The Life and Death of King Richard II*, Act ii, Scene 1.

Pilgrim's Progress.

The following excerpts are taken from "The Pilgrim's Progress", by John Bunyan.

The Pilgrims Sup with Gaius.

"So supper came up; and first, a heave-shoulder, and a wave-breast were set on the table before them . . .

"The next they brought up was a bottle of wine, red as blood . . .

"The next was a dish of milk well crumbled; but Gaius said, Let the boys have that, that they may grow thereby . . .

"Then they brought them up a dish of apples, and they were very good tasted fruit . . .

"They were presented with another dish, and it was a dish of nuts. (Song. VI, II.) Then said some at the table, Nuts spoil tender teeth, especially the teeth of children."

The Calves of My Lips.

Mercy at the Gate with "a most cruel dog thereabout".

"At last he came down to them again, and Mercy fell on the ground . . . and said Let my Lord accept of the sacrifice of praise which I now offer unto him with the calves of my lips."

Mr. Skill: Intestinal Colic.

"Now Matthew, the eldest son of Christiana, fell sick, and his sickness was sore upon him, for he was much pained in his bowels, so that he was with it, at times,

pulled as it were both ends together. There dwelt also not far from thence, one Mr. Skill, an ancient and well-approved physician . . . When he was entered the room, and had a little observed the boy, he concluded that he was sick of the gripes . . . So he made him a purge, but it was too weak . . . When Mr. Skill had seen that that purge was too weak, he made him one to the purpose . . . When this potion was prepared, and brought to the boy, he was loath to take it, though torn with the gripes as if he should be pulled in pieces. . . . It goes against my stomach, said the boy . . .

"So when the boy was healed, Christiana asked Mr. Skill, saying, Sir, what will content you for your pains and care to and of my child? And he said, You must pay the Master of the College of Physicians, according to rules made in that case and provided."

Mercy and the Shepherds.

"But Mercy being a young and breeding woman, longed for something that she saw there, but was ashamed to ask. Her mother-in-law then asked her what she ailed; for she looked as one not well. Then said Mercy, There is a looking-glass hangs up in the dining-room, off which I cannot take my mind: if, therefore, I have it not, I think I shall miscarry."

Use of the Word Caul, Meaning a Cap, Covering.

Christiana's regrets for the treatment of her husband—"rent the caul of her heart in sunder".

The Cantankerous Man.

"There's Morbid, all bile and verjuice and nerves,
Where other people would make preserves,
He turns his fruit into pickles:
Jealous, envious and fretful by day,
At night, to his own sharp fancies a prey,
He lies like a hedgehog rolled up the wrong way,
Tormenting himself with his prickles."

—Thomas Hood: "Miss Kilmansegg and her Golden Leg".

Dr. John Rutty's Diary (1753-1765).

"Tenth month, 1753.

"23.—Indulgence in bed an hour too long.

"Twelfth month, 17.—An hypochondriack obnubilation from wind and indigestion.

"Ninth month, 28.—An over-dose of whisky.

"29.—A dull, cross, cholerick day.

"First month, 1757, 22.—A little swinish at dinner and repast. Dogged on provocation.

"Second month, 5.—Very dogged or snappish.

"14th.—Snappish on fasting.

"26.—Cursed snappishness to those under me, on a bodily indisposition.

"Third month, 11.—On a provocation, exercised a dumb resentment for two days, instead of scolding.

"22.—Scolded too vehemently.

"23.—Dogged again.

"Fourth month, 29.—Mechanically and sinfully dogged."

—From "A Spiritual Diary and Soliloquies", by Dr. John Rutty, quoted by Boswell in *The Lancet*, October 19, 1907, page 1073.

A Quack Remedy.

"The introduction of this preparation and its advent into this country was heralded by a flourish of advertisement, not overloaded with, but still not altogether devoid of, that picturesque hyperbole and flamboyant mendacity which in general seem to be inseparable adjuncts to the exploitation of a nerve tonic, a hair restorer or an aperient."

—Judgement of Mr. Justice Eve, *British Medical Journal*, June 7, 1913, page 1240.

Duke of Lauderdale's Heart.

"All these things, together with a load of age and of a vast bulk, sunk Duke Lauderdale, so that he died that summer [in 1682]. His heart seemed quite spent: there was not left above the bigness of a walnut of firm substance: the rest was spungy, liker the lungs than the heart."

—Gilbert Burnet: "History of His Own Time", Volume II, page 340.

Inoculation for the Smallpox.

"The devastation of the small-pox when it visits places where it comes seldom, is well known. He (the Laird) has disarmed it of its terror at Muach, by innoculating eighty of its people. The expence was two shillings and sixpence a head."

—Samuel Johnson: "A Journey to the Western Islands", 1773.

Cadaveric Rigidity.

A good example of the almost instantaneous onset of cadaveric rigidity is given by A. W. Kinglake in "The Invasion of the Crimea", Volume V, page 220, in describing the Battle of Balaclava, in which he gives the following account of the death of Captain Nolan:

"But a Russian shell bursting on the right front of Lord Cardigan now threw out a fragment which met Nolan full on the chest and tore a way into his heart. The sword dropt from his hand; but the arm with which he was waving it the moment before still remained high uplifted in the air, and the grip of the practised horseman remaining as yet unrelaxed still held him firm in his saddle. Missing the perfect hand of his master, and finding the accustomed governance now succeeded by dangling reins, the horse all at once wheeled about, and began to gallop back upon the front of the advancing brigade. Then from what had been Nolan—and his form was still erect in the saddle, his sword-arm still high in the air—there burst forth a cry so strange and appalling that the hearer who rode the nearest to him has always called it 'unearthly'. The firm-seated rider, with arm uplifted and stiff, could hardly be ranked with the living. The shriek men heard rending the air was scarce other than the shriek of a corpse. This dead horseman rode on till he had passed through the interval of the 13th Light Dragoons. Then at last he dropt out of the saddle."

Scurvy.

"Soon after our passing Straits Le Maire, the scurvy began to make its appearance amongst us . . . The mortality went on increasing, and the disease extended itself so prodigiously, that after the loss of above two hundred men, we could not at last muster more than six fore-mast men in a watch capable of duty.

"This disease, so frequently attending all long voyages, and so particularly destructive to us, is surely the most singular and unaccountable of any that affects the human body. For its symptoms are inconstant and innumerable, and its progress and effects extremely irregular: for scarcely any two persons have the same complaints, and where there hath been some conformity in the symptoms, the order of their appearance has been totally different. However, though it frequently puts on the form of many other diseases, and is therefore not to be described by any exclusive and infallible criterions; yet there are some symptoms which are more general than the rest; and therefore, occurring the oftenest, deserve a more particular enumeration. These common appearances are large discoloured spots dispersed over the whole surface of the body, swelled legs, putrid gums, and, above all, an extraordinary lassitude of the whole body, especially after any exercise, however inconsiderable; and this lassitude at last degenerates into a proneness to swoon on the least exertion of strength, or even on the least motion.

"This disease is likewise usually attended with a strange dejection of the spirits, and with shiverings, tremblings, and a disposition to be seized with the most dreadful terrors on the slightest accident. Indeed it was most remarkable, in all our reiterated experience of this malady, that whatever discouraged our people, or at any time damped their hopes, never failed to add new vigour to their distemper; for it usually killed those who were in the last stage of it, and confined those to their hammocks who were

before capable of some kind of duty; so that it seemed as if alacrity of mind, and sanguine thoughts, were no contemptible preservatives from its fatal malignity.

"But it is not easy to complete the long roll of the various concomitants of this disease; for it often produced putrid fevers, pleurisies, the jaundice, and violent rheumatic pains, and sometimes it occasioned an obstinate costiveness, which was generally attended by a difficulty of breathing; and this was esteemed the most deadly of all the scorbutic symptoms; at other times the whole body, but more especially the legs, were subject to ulcers of the worst kind, attended with rotten bones, and such a luxuriancy of fungous flesh, as yielded no remedy. But a most extraordinary circumstance, and what would be scarcely credible upon any single evidence, is, that the scars of wounds which had been for many years healed, were forced open again by this virulent distemper: of this, there was a remarkable instance in one of the invalids on board the Centurion, who had been wounded about fifty years before at the battle of the Boyne; for though he was cured soon after, and had continued well for a great number of years past, yet on his being attacked by the scurvy, his wounds, in the progress of his disease, broke out afresh, and appeared as if they had never been healed: nay, what is still more astonishing, the callus of a broken bone, which had been completely formed for a long time, was found to be hereby dissolved, and the fracture seemed as if it had never been consolidated. Indeed, the effects of this disease were in almost every instance wonderful; for many of our people, though confined to their hammocks, appeared to have no inconsiderable share of health, for they ate and drank heartily, were cheerful, and talked with much seeming vigour, and with a loud strong tone of voice; and yet on their being the least moved, though it was only from one part of the ship to the other, and that in their hammocks, they have immediately expired; and others, who have confided in their seeming strength, and have resolved to get out of their hammocks, have died before they could well reach the deck; and it was no uncommon thing for those who were able to walk the deck, and to do some kind of duty, to drop down dead in an instant, on any endeavours to act with their utmost vigour: many of our people having perished in this manner during the course of this voyage."

—George Anson: Anson's "Voyage Round the World", Book I, Chapter x, page 31.

1740-1744. After doubling Cape Horn; account by "Richard Walter, M.A." on title page, but probably by "Benjamin Robins, a celebrated engineer-officer".

Scurvy on the Voyage to Goa in India in 1579.

"And by reason of the long navigation and want of food and water they fall into sundry diseases; their gums wax great and swell and they are fain to cut them away, their legs swell and all the body becometh sore, and so benumbed that they cannot stir hand nor foot, and so they die for weakness. Others fall into fluxes and agues and die thereby."

—Letter of the Jesuit Thomas Stevens to his father (J. C. Locke: "The First Englishmen in India", page 27).

The Gold Road—Across the Isthmus of Panama. Yellow Fever and Malaria.

"It was from a hill on the Isthmus that de Balboa discovered the Pacific Ocean. From a like height Sir Francis Drake gazed upon that alluring sea—the first Englishman whose eyes had ever been greeted by the sight of it.

"It was at Nombre de Dios on the Isthmus that Drake first made himself "redoubtable to the Spaniards", while the most famous deeds of the Buccaneers and their most venturesome assaults belong to the annals of this fever-stricken land.

"Across the Isthmus was carried year after year, partly by mule trains and partly by river, the incredible wealth of Peru.

"During all these toiling years, Death has stood in the narrow crossing and has there exacted toll from whomsoever passed by the way.

"The loss of life involved in the construction of the little line of rail was alone appalling. The iron road moved across the land like the car of Juggernaut, crushing to death all living things it came upon. It has been said, and probably with truth, that every tie or sleeper beneath the rails cost a human life.

"Enriquez de Guzman, who came into these parts in 1534, asserts that out of every hundred men who went to Peru for gold, eighty never returned again.

"In like manner, during the gold craze in California, the number who met with death on the Isthmus, within sight of the sea that was to carry them and their nuggets home, would have filled many a happy town.

"Last of all, during the construction of the canal by the French Company, men died yearly not in hundreds but in thousands. In truth there is no burial ground comparable with this on the face of the earth, for the dead lie thicker than the trees."

—Sir Frederick Treves: "The Cradle of the Deep", page 310.

Exposure to the Tropical Sun.

"One reason why I could not go quite naked was, I could not bear the heat of the sun so well when quite naked, as with some clothes on—nay, the very heat frequently blistered my skin; whereas, with a shirt on, the air itself made some motion, and, whistling under the shirt, was two-fold cooler than without it; no more could I ever bring myself to go out in the heat of the sun without a cap or a hat; the heat of the sun beating with such violence as it does in that place, would give me the headache presently, by darting so directly on my head, without a cap or hat on, so that I could not bear it; whereas, if I put on my hat, it would presently go away."

—Daniel Defoe: "The Life and Adventures of Robinson Crusoe", page 124.

Ambroise Paré and the Battlefield.

"We saw more than half a league round us the earth all covered with the dead; and hardly stopped there, because of the stench of the dead men and their horses; and so many blue and green flies rose from them, bred of the moisture of the bodies and the heat of the sun, that when they were up in the air, they hid the sun. It was wonderful to hear them buzzing; and where they settled, there they infected the air, and brought the plague with them. *Mon petit maistre*, I wish you had been there with me, to experience the smells, and make report thereof to them that were not there."

—Stephen Paget: "Journeys in Divers Places", page 94 (Battle of Saint Quentin, 1557).

"The camp broken, I returned to Paris, with my gentleman whose leg I had cut off; I dressed him and God cured him. I sent him to his house, merry, with a wooden leg, and he was content saying that he had got off cheap, not to have been miserably burned to stop the blood, as you write in your book, *mon petit maistre*."

—Francis R. Packard: "Life and Times of Ambroise Paré", "Apology and Treatise", page 189.

Of Monsieur de Pienne: "He was trepanned at the side of the temporal muscle, on the frontal bone, I dressed him, with other surgeons, and God cured him, and to-day he is still living, thank God."

—Francis R. Packard: "Life and Times of Ambroise Paré", "Apology and Treatise", page 198.

The King's Evil.

"It was suggested by some confident spirits that the Queen's title should be tested by affording to her the opportunity of proving whether she inherited the one miraculous gift peculiar to the legitimate occupant of the English throne—it had been bestowed on the holy saint Edward the Confessor, and was intrusted to his successors as a testimony that God sanctioned the right of inheritance claimed by them. Would her Majesty condescend to touch for the king's evil? It was done accordingly. From a

crowd of applicants for the distinction of being handled by royalty, a selection by skilled physicians was made of those hapless beings who, beyond the aid of physical remedies, were the proper objects of the miraculous intervention of the sovereign."

Of these Samuel Johnson was one, and he remembered the ceremony. The touch was found to be successful. The announcement that it was so gladdened many a loyal subject and ardent churchman, rejoicing and trembling in mysterious awe at the wonderful way of Providence. This was no technical confirmation of a parliamentary title—it was God's doing, and wonderful in their sight.

"Bath, October 6th—A great number of persons coming to this place to be touched by the Queen's Majesty for the evil, her Majesty commanded Dr. Thomas Gardner, her chief surgeon, to examine them all particularly, which accordingly was done by him, of whom but thirty appeared to have the evil, which he certified by tickets as is usual, and these thirty were all touched that day."

—J. H. Burton: "The Reign of Queen Anne", Volume II, page 202.

Old Age.

"Remember now thy Creator in the days of thy youth, while the evil days come not, nor the years draw nigh, when thou shalt say, I have no pleasure in them;

"While the sun, or the light, or the moon, or the stars, be not darkened; nor the clouds return after the rain:

"In the day when the keepers of the house shall tremble, and the strong men shall bow themselves, and the grinders cease because they are few, and those that look out of the windows be darkened,

"And the doors shall be shut in the streets, when the sound of the grinding is low, and he shall rise up at the voice of the bird, and all the daughters of music shall be brought low:

"Also when they shall be afraid of that which is high, and fears shall be in the way, and the almond-tree shall flourish, and the grasshopper shall be a burden, and desire shall fail; because man goeth to his long home, and the mourners go about the streets:

"Or ever the silver cord be loosed, or the golden bowl be broken, or the pitcher be broken at the fountain, or the wheel broken at the cistern.

"Then shall the dust return to the earth as it was; and the spirit shall return unto God who gave it."

Ecclesiastes, Chapter XII, Verses 1 to 7.

"For to degenerate and die is as normal as to be developed and live; the expansion of growth and the full strength of manhood are not more natural than the decay and feebleness of a timely old age: not more natural, because not more in accordance with constant laws, as observed in ordinary conditions. As the development of the whole being, and of every element of its tissues, is according to certain laws, so is the whole process regulated by which all that has life will, as of its own workings, cease to live. And as in healthy development and growth all parts concur in equivalent changes, so in the natural decline of life do all parts change in equivalent degenerations, till all together cease to be capable of living. For it is natural to become feeble and infirm, to wither and shrivel, to have dry, dusky, wrinkled skins and greasy brittle bones, to have weak fatty hearts, blackened inelastic lungs and dusky thin stomachs, and to have every function of life discharged feebly, and, as it were, wearily; and then, with powers gradually decreasing, to come to a time when, all the functions of bodily life ceasing to be discharged, death, without pain or distress, ensues."

—Sir James Paget: "Lectures on Surgical Pathology", Third Edition, 1870, page 70.

"Some people as they grow old seem only to wither and dry up; sharp-featured, shrivelled, spinous old folk, yet withal wiry and tough, clinging to life, and letting death have them, as it were, by small instalments slowly paid. Such are the 'lean and slippered pantaloons'; and their 'shrunk shanks' declare the pervading atrophy.

"Others, women more often than men, as old and as ill-nourished as these yet make a far different appearance. With these the first sign of old age is that they grow fat; and this abides with them till, it may be, in a last illness sharper than old age, they are robbed even of their fat. These, too, when old age sets in, become pursy, short-winded, pot-bellied, pale, and flabby; their skin hangs, not in wrinkles, but in rolls; and their voice, instead of rising 'towards childish treble', becomes gruff and husky."

—Sir James Paget: "Lectures on Surgical Pathology", Third Edition, 1870, page 82.

Falstaff Before the Chief Justice.

"*Chief Justice.* Do you set down your name in the scroll of youth, that are written down old with all the characters of age? Have you not a moist eye? a dry hand? a yellow cheek? a white beard? a decreasing leg? an increasing belly? Is not your voice broken? your wind short, your chin double? your wit single? and every part about you blasted with antiquity and will you yet call yourself young? Fie, fie, fie, Sir John!"

—Shakespeare: Second Part of *King Henry IV*, Act I, Scene 2.

Death of Falstaff.

"*Hostess.* . . . he is so shaken of a burning quotidian tertian that it is most lamentable to behold."

—Shakespeare: *King Henry V*, Act II, Scene 1.

"*Hostess.* . . . 'A made a finer end, and went away, an it had been any christom child; 'a parted even just between twelve and one, even at the turning o' the tide: for after I saw him fumble with the sheets, and play with flowers, and smile upon his fingers' ends, I knew there was but one way; for his nose was as sharp as a pen, and 'a babbled of green fields. *How now, Sir John!* quoth I: *what, man! be o' good cheer.* So 'a cried out—*God, God, God!* three or four times. Now I, to comfort him, bid him 'a should not think of God; I hoped there was no need to trouble himself with any such thoughts yet. So 'a bade me lay more clothes on his feet; I put my hand into the bed and felt them, and they were as cold as any stone; then I felt to his knees, and so upward, and upward, and all was as cold as any stone."

—Shakespeare: *King Henry V*, Act II, Scene 3.

A METHOD FOR THE REMOVAL OF TONSILS AND ADENOIDS UNDER LOCAL ANÆSTHESIA WITH THE PATIENT IN THE RECUMBENT POSITION.

By R. H. BETTINGTON,
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THE technique to be described was developed in the Australian Imperial Force in 1940, and has been used for the last two years at the 113th Australian General Hospital. A similar method may have been employed previously by others, but I have seen no description of it published.

Dr. D. G. Perrett, of Newcastle, first called my attention to the fact that the Boyle Davis gag can be utilized for local anæsthesia. I tried it first when attached to the 2/1 Australian General Hospital at Gaza Ridge, Palestine. A full description of the whole procedure, actual operative details being omitted, is set out below.

Premedication.

All patients are given thirty grains of potassium bromide and ten minims of syrup of chloral on the evening previous to operation. Prior to operation, any one of the following schemes of dosage may be used:

1. One-quarter of a grain of morphine and one one-hundredth of a grain of hyoscine one hour before operation.

2. One-twelfth of a grain of morphine and one one-hundred-and-fiftieth of a grain of hyoscine two hours before operation. One-quarter of a grain of morphine and one one-hundred-and-fiftieth of a grain of hyoscine one hour before operation.

3. One-sixth of a grain of morphine and one one-hundred-and-fiftieth of a grain of hyoscine two hours before operation. One-quarter of a grain of morphine and one one-hundred-and-fiftieth of a grain of hyoscine one hour before operation.

The body weight of the patient is the criterion for dosage. The first scheme is used for the majority of women and for small men, the second scheme for large women and for the majority of men, and the third scheme for men of exceptional size.

Pre-Operative Spraying.

Any local anæsthetic suitable for application to a mucosal surface may be used as a spray. It is applied from a spray having a swivel nozzle, with the patient sitting up. My own habit has been to use a mixture of 10% cocaine solution with a 1 in 1,000 solution of adrenaline hydrochloride, the relative proportions being as six is to four. Provided the patient is required to spit after every period of spraying—four or five puffs—the danger of cocaine reaction is negligible. The first spraying is done ten minutes before operation in the following order: (i) the dorsum of the tongue where the gag spatula is to exert pressure; (ii) the anterior tonsillar pillars of both sides; (iii) the post-nasal space, with the nozzle turned up; (iv) the lower tonsillar poles and the top of the glottis, with the nozzle turned down. If the upper jaw is edentulous, the gum surface, where the gag makes contact, should be sprayed.

The procedure is repeated five minutes after the first application; the patient is then prepared for operation.

Position of the Patient.

The patient is placed in the recumbent position, with a small pillow under the shoulders, so that the post-nasal space is at a lower level than the glottis. The height of this pillow will vary with the size of the patient and the length and flexibility of the neck. The Boyle Davis gag is now put in position with the spatula as near as possible to the mid-line, and the free end is kept elevated by a metal jack, or by a rectangular block of light wood, which can be cut to a suitable size. I use a set from which the anæsthetic pipes have been removed; thus more space is allowed for manipulation.

Injection.

All those who practise tonsillectomy under local anæsthesia will have their own preference for the solution to be used and the sites for injection. I use 15 to 20 millilitres of a 0·5% solution of "Novocain", 10 minims to the ounce of a 1 in 1,000 solution of adrenaline hydrochloride being added. The sites of injection, according to my plan, are as follows.

1. Attach a curved needle and give an injection along the posterior pillars and behind the upper and lower poles. Again with a curved needle give an injection under the mucosa of the anterior pillars and around the upper curve near the uvula.

2. Grasp each tonsil in turn with holding forceps and draw gently toward the mid-line, thus identifying the lateral border. With a straight needle make three injections behind the upper pole, the centre and the lower pole.

3. Still using a straight needle, give an injection through the lower pole into the base of the tongue.

Adenoids.

If adenoids are present, the injections are made with the curved needle before the tonsil operation has been commenced. The needle is introduced under the mucosa of the posterior naso-pharyngeal wall and pushed up towards the skull vertex until the point impinges on the bone of the skull base. The plunger is gently pushed in while the needle is being slowly withdrawn. This injection is made three times in the mid-line and along each lateral wall.

When the first tonsil has been removed a twelve-inch length of one-inch ribbon gauze is soaked in the cocaine and adrenaline mixture, wrung out and packed into the post-nasal space. After the tonsil removal has been completed, this pack is removed and the adenoids are curetted out.

Comment.

I do not propose to discuss the relative merits of local and general anæsthesia for tonsillectomy. I shall say only this: ten years ago I had removed only a few tonsils under local anæsthesia, but now I try to persuade all adult patients to submit to this procedure. During more than five years in the army I performed nearly six hundred tonsillectomies, and in only eight of these was a general anæsthetic required.

Reviews.

A YEAR BOOK ON GENERAL SURGERY.

LIKE its predecessors in recent years, "The 1945 Year Book of General Surgery" has been edited by Evarts A. Graham.[1] The book is arranged in many sections. The first deals with anæsthesia and analgesia, and then follow sections on asepsis and antisepsis, operative technique, military surgery, wound healing and pathological conditions, tumours, blood vessels, bones and fractures. From this point onwards the sections deal with regions or organs. There is one exception—a section on hernia is introduced after the section on the large bowel. This may not be quite logical, but from the practical point of view it makes the subject easier to handle.

Under the first heading of anæsthesia and analgesia appears a reference to what must be regarded as a preliminary report on the intravenous use of "Novocain" as a substitute for morphine in post-operative care. Curare, which is being used in order to secure muscular relaxation in anæsthesia, is discussed—two papers on the subject are abstracted. In the section on asepsis and antisepsis an important reference is that to a study by F. L. Meleney on the use of sulphonamides in the prevention of wound sepsis. The review by H. R. G. Poate on the acridines is also mentioned. The work of Large and Heinbecker and of Bruneau and Heinbecker on the effects of cooling on wound healing and experimentally infected wounds is regarded by the editor as important; it is mentioned in connexion with wound healing and in the section devoted to the upper extremity. Under wound healing, too, skin grafting by various methods is discussed at some length. The use of penicillin in the treatment of open fractures of the femur is described; the penicillin did not control sepsis fully, and the conclusion is that its use is not a substitute for surgery. This is one report. According to another, early wound suture and the use of penicillin in 62 fractures (site not specified) were immediately successful in 58 cases. Penicillin is mentioned in connexion with injuries to the brain and meninges. In the section on the thyreoid the repeated reference to thiouracil shows how this drug has become part of the surgeon's armamentarium. In the section on the breast there are three reports dealing with the effects of surgical and X-ray castration on mammary cancer. Results are reported for both women and men; they were temporary, but much more striking among men than among women. In the section on the surgery of tuberculosis the results reported in this journal by C. G. Bayliss on closed intrapleural pneumonolysis are given; results by F. D. Stubbs, of Philadelphia, are also included. Turning to the abdomen, we find reference to peritoneoscopy as a useful procedure in certain doubtful cases. Wangensteen's views on the clinical aspects of the peptic ulcer problem are given due consideration. The references to peptic ulcer are many and cover most aspects of the subject, at any rate from the surgical point of view. E. F. Berman has devised a "simplified method of defunctionalizing the colon" according to the precepts of Devine. He uses only a colostomy in any portion of the colon proximal to the lesion and a special double lumen tube with a balloon attached—one portion of the bowel is functionally divorced from the other by these means. In the section on the pancreas two cases of rupture of the pancreas are reported; rupture was caused by violence and no other viscera were

[1] "The 1945 Year Book of General Surgery", edited by Evarts A. Graham, A.B., M.D.; 1946. Chicago: The Year Book Publishers Incorporated. Melbourne: W. Ramsay (Surgical) Proprietary Limited. 7" × 4¾", pp. 736, with illustrations. Price: 24s.

injured. The section on the spleen contains several reports on rupture of that organ. Among the cases mentioned are several in which rupture was delayed; in one instance rupture occurred four months after injury was sustained. The confusion that may exist between root neuritis and appendicitis is described in the section on the spine and spinal cord.

It would be possible to refer to many more subjects of interest in this year's year book on surgery. Those that have been named will show that this year's volume is worth a place on the shelves of every practitioner concerned with surgical work.

PROGRESS IN PÆDIATRICS.

THE important work carried out in the field of pædiatrics during 1945 is reviewed in "The 1945 Year Book of Pediatrics",[1] edited by Isaac A. Abt, with the collaboration of Arthur F. Abt. The references to writings of different authors are grouped under sectional headings; some of the headings refer to systems or regions of the body, others refer to certain diseases or groups of diseases, and others again to such general subjects as nutrition, surgery, therapeutics and toxicology. There is a good subject index which makes reference to a particular subject a simple matter. The book may thus be used as a work of reference or as one in which the reader may browse to his heart's content.

This book containing such a wealth of material, it is impossible to give an adequate idea of its contents and difficult to select subjects to which attention should be drawn. There are many references to meningitis in its different forms; among the work included is that on influenzal meningitis by Elizabeth K. Turner, of the Children's Hospital, Melbourne. There are some important references to mumps—its association with chicken-pox, and reports on work in immunity in connexion with it. Further reports on the occurrence of abnormalities in infants following maternal rubella are recorded. In the section on rheumatism discussions on the use of penicillin appear and reference is also made to the prevention of recurrences by use of sulphonamide drugs. There are several references to *erythroblastosis fœtalis*. The section on tuberculosis includes an account of the pathological anatomy of the primary complex and also of chronic disseminated tuberculosis. Diarrhœal diseases have been discussed by several authors; the dysentery bacillus was responsible in some instances, in others, such as the epidemic diarrhœa reported by Kate I. Campbell, the causative organism was not isolated. Nephrectomy has been undertaken in the treatment of a two and a half year old child on account of hypertension, and after three years the child is apparently cured; a kidney was also removed for the same reason from a child aged seven years, and after five years the blood pressure remains normal and the cure is thought to be permanent. In the section on therapeutics and toxicology there are many references to sulphonamide therapy and to the use of penicillin.

This book should engage the attention of every pædiatrician and indeed of every general practitioner.

PROGRESS IN OBSTETRICS AND GYNÆCOLOGY.

ALL practitioners interested in obstetrics and gynæcology will welcome the appearance of "The 1945 Year Book of Obstetrics and Gynecology", which is one of the books of the Practical Medicine Series.[2] The editor is J. P. Greenhill. In this book will be found a short summary of work done during the year in both subjects. These subjects are suitably grouped together. In the opening pages of the part of the volume devoted to gynæcology (the second part of the book) will be found reference to an article by J. Pon Orfila, who holds that obstetrics and gynæcology should be unified into one specialty and designated gynæcology. The editor in a note (it is longer than the abstract of the paper by Orfila) states that Orfila suggested that the year book should be known as the "Year Book of Gynecology" and be divided into three sections devoted to "general gynecology", "extragravid gynecology", and "obstetric gynecology". The editor discusses the subject at some length and comes to the conclusion that everyone who contemplates practising obstetrics or gynæcology, as those terms are now used, should without fail be trained in both specialties. With this contention most people who have thought about the subject will agree.

Another paper to which attention should be drawn is that of W. R. Cooke, who deals with the differential psychology of the American woman. The psychology of the American woman is not very different, if at all, from that of woman in any English-speaking country. There is no doubt that many symptoms peculiar to women are purely of mental origin. Psychotherapy is needed if relief from symptoms is to be obtained. Without going further into Cooke's argument we may agree that to be successful in affording relief to his patients an obstetrician or a gynæcologist must be a good psychologist.

With these introductory remarks we may describe shortly the general structure of this year book. The part dealing with obstetrics is divided into four main sections. The section on pregnancy is divided into four subsections on physiology, abortion, complications and toxæmia. The second section on labour deals in turn with general considerations, analgesia and anæsthesia, complications, operative obstetrics and uterine hæmorrhage. The third section on the puerperium deals with general considerations and infection; the fourth section is devoted to consideration of the newborn.

The part of the book covering gynæcology has sections on general principles, diagnosis, infertility, ectopic pregnancy, operative technique, benign tumours, malignant tumours, special tumours of the ovary, menstruation and its disorders, endocrinology and infections.

These subjects are, as in all books of this series, covered by abstracts from articles that have appeared in medical journals in different countries. To many of the abstracts the editor has added an editorial note; in this regard he has been most liberal. In our opinion this adds considerably to the value of the book which may be recommended to readers with the greatest confidence.

NUTRITION AND CHEMICAL GROWTH IN CHILDHOOD.

VOLUME I of "Nutrition and Chemical Growth in Childhood", which appeared about four years ago, presented the "evaluation" of a mass of data which related to the growth and development of some twenty normal children. Volume II was to have been the interpretation of this material. However, the workers came to the conclusion that because future advances might enable other interpretations than theirs to be placed upon the data, it was desirable to present in full the results of all experiments and all observations made upon their subjects. The present volume contains this material.[1]

The observations on some children lasted from shortly after birth to the age of fourteen or fifteen years. In other cases the period was shorter and covered various intervals between these limits. Each child was studied at regular intervals, in some instances weekly, and the material in the present volume includes height, weight and other anthropometric data, blood counts, plasma nitrogen and mineral content, basal metabolism measurements, records of size of the bones of the wrists *et cetera*, and constituents of the urine including nitrogen partition. A large number of radiographs of wrist, jaw, teeth, pelvis, knee and foot, and of the progress of barium meals through the gastro-intestinal tract have been included. In addition, the full protocols of each balanced experiment for each child have been reported.

It is understood that the book cost more than the published price to produce, and that the difference was met from special funds at the disposal of the author.

This book undoubtedly has a place in a large reference library or perhaps on the shelf of a pædiatrician; but it is not recommended as a useful addition to the library of the general practitioner.

[1] "The 1945 Year Book of Pediatrics", edited by Isaac A. Abt, D.Sc., M.D., with the collaboration of Arthur F. Abt, B.S., M.D., Comdr., M.S., U.S.N.R.; 1946. Chicago: The Year Book Publishers, Incorporated. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 7" × 4½", pp. 448, with many illustrations. Price: 24s.

[2] "The 1945 Year Book of Obstetrics and Gynecology", edited by J. P. Greenhill, B.S., M.D., F.A.C.S.; 1946. Chicago: The Year Book Publishers Incorporated. 7" × 4½", pp. 576, with illustrations. Price: 24s.

[1] "Nutrition and Chemical Growth in Childhood", by Icie G. Macy, Ph.D., Sc.D., with a foreword by Lawrence Reynolds, M.D., and a supplement by Julia Outhouse Holmes, Pr.D.; Volume II, original data; 1946. Springfield: Charles C. Thomas. 9" × 6", pp. 1043, with many illustrations. Price: $10.00.

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CEREBRAL TRAUMA AND ITS MECHANISMS.

THE clinician meets few, if any, more difficult problems than that connected with cerebral involvement in head injury. War surgery has given surgeons wide experience of penetrating wounds of the skull. As a result, not only has the application of modern methods of treatment saved many lives that would previously have been lost, but the relationship between trauma and symptoms has become less obscure. In cerebral injury from blunt mechanical trauma the greatest difficulty arises. The trouble is that the skull is not a regularly shaped, homogeneous body and the effect of a force acting upon it depends on many factors. The effects may be immediate or remote, and the immediate effects may be of such a kind that they are recognizable on macroscopic examination of the brain; on the other hand, they may not be obvious. In these circumstances they may sometimes be detected on microscopic examination, and, again, cases occur in which no cause of death can be discovered. The literature on the subject, which is extensive, has been reviewed recently by C. D. Tedeschi,[1] who holds that a physical visualization of the ways by which injuring forces are transmitted to the brain is essential if the problem of cerebral trauma is to be approached correctly.

The patterns of fracture of the skull, although subject to some extent to the laws of mechanics, are varied and unpredictable because the skull is composed of panels of bone, offering variations both in thickness and in elasticity from race to race, from individual to individual, and in the same individual in the different portions of the skull. This statement is equally true of cerebral injuries caused by physical violence, and in this regard it has to be remembered that the brain is composed of tissues that differ in specific gravity, toughness and tensile strength. In relation to the mechanism of movement, brain injuries have been said to occur either by distortion of the skull (the "compression concussion" of Brown and Russell), or by movements of the brain within the skull as the head is thrown through space and then brought to a sudden rest (the "acceleration concussion" of the same authors). In compression concussion the skull is likely to undergo momentary local deformation at the site of application of the force and also general distortion. The new curvatures of the distorted skull will impinge on the underlying brain matter, giving rise to increased pressure in some areas and to diminished pressure in others. The architecture of the skull has a great deal to do with the extent of the injury. The rebounding of the skull is also important. As it occurs the meningeal vessels may be pulled away from the brain and broken and the superficial brain structures may sustain further damage. When the forces of acceleration are operating damage may be more severe. Not only is the brain damaged at the area where the force is applied, but the brain is made to slide within its dural covering and single anatomical units and perhaps the individual cerebral cells are likely to be distorted and the connecting pathways to be bent, stretched or torn. Blood vessels may be torn or cranial nerves evulsed. Brown and Russell have shown that if the head is prevented from moving at the moment of the blow, no concussion occurs; if even slight movements are allowed concussion takes place. Holbourn has explained this by showing that to produce shear strains of the skull a rotary acceleration is necessary. Localized damage in cranio-cerebral injury is attributed to skull distortion and distant damage to rotation of cerebral tissue around regions where the brain is fixed locally in relation to the skull. As a result of this rotation constituent particles of the brain are pulled apart; if normal relations are not restored when the blow is over, nervous symptoms become manifest. Thus, concussion is thought to be due to a minimal degree of separation of constituent particles and contusion to a maximal separation. Most practitioners would possibly overlook the fact that the smaller the area over which the energy of the impact is discharged, in a fixed unit of time, the greater will be its intensity. If the area of impact is reduced, a point is reached at which the injuring body penetrates the skull. This happens with a gunshot wound. The penetration lessens the degree of acceleration to which the skull is subjected. This explains why, although penetrating wounds often cause severe local damage to the brain, they often fail to cause concussion.

Tedeschi deals in an interesting way with the question of contralateral injury, or injury by *contre-coup*, as it is often called. Use of this term generally means that a pole of the brain opposite the site of impact has received some damage. Some interesting suggestions have been made of the way in which this damage is caused. One suggestion is that the energy of impact is propagated by irradiating waves of motion through meridional lines which diverge as they leave the site of impact and converge as they approach the opposite pole. At the point of collision of the converging waves a contralateral injury is likely to occur. This view is put forword by Moritz. Another possibility is that there are two impacts, the first at the site of the blow and the second where the advancing surfaces of the brain are brought to a sudden rest by the forces which resist its forward motion. A third possible cause is the shortening of the axis of the brain along the direction of the travelling force. Tedeschi remarks that

[1] *Medicine*, December, 1945.

this last-mentioned mechanism can apply to impacts on the sides of the head because of the relatively high degree of elasticity of the horizontal arch of the skull. It does not appear, however, to apply to occipital or frontal impacts. The construction of the longitudinal arch of the skull and the rigidity of the bones at the base are sufficient explanation of this. Ritchie Russell holds that traction rather than contusion is the actual cause of contralateral injury, as the brain is torn from its coverings by the force of its own momentum and the pia-arachnoid membranes and blood vessels are stretched and torn. Tedeschi agrees that this hypothesis explains contralateral subarachnoid bleeding, but holds that it does not account for the extensive laceration of cortex and membranes that is so often seen. He concludes that contralateral injuries may result from different mechanisms which, according to the modality of the accident, may operate singly or in combination. It is therefore, he thinks, correct to use the term contralateral injury in a limited sense to indicate only that an area of the brain opposite the site of impact has been injured.

This short account gives an outline of Tedeschi's review of the mechanisms of cerebral trauma. It by no means covers the whole of his review which deals in full with the subject of cerebral injury "by blunt mechanical trauma". A discussion on these mechanisms is far from being purely academic. If a clinician has an understanding of the process which has probably taken place in the cranium of his patient, he is at least starting off on the right foot in the investigation of his condition. Tedeschi remarks that the effects of a trauma "will vary according to the area of application of the striking force, the degree of plasticity, elasticity, and tensile strength of the part struck, the shape, speed and weight of the injuring agent, and the degree of relaxation of the offended part at the moment of the impact". The clinician may not be able to determine these factors, but he can try. In making this attempt he will be bound to think of the immediate morphological effects of trauma and the microscopic changes that may take place, subjects that are covered in Tedeschi's review; he will also not fail to remember the most important group of cerebral traumata not associated with recognizable organic changes, also described by Tedeschi. Needless to say, the most careful record of all signs and symptoms should be kept in every case of head injury. It is held that the care of patients with fractures of the limbs should be in the hands of a trained expert in the subject. With equal justification it can be held that the progress of every patient with a cerebral injury should be observed by a trained neurologist. If the patient dies, a post-mortem examination, including the preparation and microscopic examination of sections, should be undertaken. In no other way can knowledge of this subject grow.

Current Comment.

DIAGNOSTIC METHODS IN CARDIAC DISEASE.

A GREAT deal is now heard about mechanization in all fields of human interest. A good debate can always be started between the present and past generations of doctors on the merits and demerits of special investigation in medicine, for it is often hard to see where the distinction is to be drawn between the research value and the clinical value of laboratory procedures. Since the introduction of the electrocardiograph into clinical medicine and the consequent simplification of the instrument it is natural that its use is becoming almost a routine procedure. Therefore it is of interest to read a brief address by Fredrick A. Willius, of the Mayo Clinic, delivered to the Section of Medicine at the meeting of the Canadian Medical Association last year.[1] With commendable restraint Willius wonders whether mechanical methods of detection are receiving over-emphasis at the expense of other well-tested methods. Everyone will agree that his contention that a careful clinical history must be taken in every case and followed by a thorough and complete physical examination is an axiom. All other methods are adjuncts and the question of their employment in any given case is a matter for individual decision. In some cases the need for such adjuncts is small, as in rheumatic carditis. In others the evidence is not so convincing by itself. Willius remarks that in the anginal syndrome of coronary sclerosis the clinical history is frequently all that can be relied upon for a diagnosis, as the heart may not show any abnormality on ordinary examination or on fluoroscopy, while the electrocardiogram shows no significant alterations in about a third of the cases. The tracings suggestive of or characteristic of coronary occlusion or of ventricular strain are of course most important when found. In chronic constrictive pericarditis Willius gives an example of the need for integration of all the evidence, for here, although the onset is suggestive, clinical and even radiological examination of the heart itself may not supply the clue unless calcification is demonstrated and there is no pathognomonic electrocardiographic pattern. In this case careful study of the secondary phenomena is of prime importance. These examples are cited by the author in order to reinforce his expressed view that the advent of what he calls a new order of being, the electrocardiographer, has brought a false set of values into cardiac diagnosis in some quarters. The danger lies with the practice of making a clinical diagnosis on the basis of the electrocardiogram, an act of faith in which Willius aptly remarks that the electrocardiographer exerts his talents far beyond the boundaries of the science. It is contended that the physician who refers the patient expects a clinical diagnosis, but Willius points out that there are two alternatives to the interpreter of the record: either he must ensure that his colleagues who seek his opinion understand clearly the limitations of the method or he must permit them to draw their own conclusions. The attitude that is adopted in most large medical centres in this country is surely that the mechanical aberrations shown on the tracing are noted and measured, and an indication is given of the general conformity of the pathological pattern to certain clinical conditions. It is felt by most physicians that where an electrocardiogram is taken as part of an attempt to assess the condition of the heart, either the medical practitioner responsible for advising the patient should be able to sum up the total information gained or else the opinion should be sought of someone who is able to do so. When the electrocardiogram shows no abnormality this is of particular importance. But it must be admitted that the machine is still made the supreme arbitrator in too many cases, and senior medical men who have had recent service experience will agree that it is not only in civilian practice that this occurs. Indeed we understand that instructions were given at one time that a clinical opinion in cardiac cases was only to be appended to the general history and not recorded on the electrocardiogram, so as to avoid the bias that might arise in subsequent dealings with the patient in his later medical adventures.

Willius is careful to point out the great advances that have been made in the localization of cardiac infarcts and the occasional recognition of a picture suggestive of pulmonary infarction, but he also reminds us that the authorities who have described these electrocardiographic signs have clearly stated that the characteristic tracings may not appear or may be modified or delayed. It is also important to remember that there may be more than one pathological process at work, a composite picture thus being

[1] *The Canadian Medical Association Journal*, March, 1946.

produced in the electrocardiogram. Willius ends by stating that until the fallacious practices he has condemned are stopped, the future of electrocardiography is uncertain. Of course, it is not the fault of the medical profession alone if the public have a wrong perspective in this matter of special methods which should be ancillary to clinical medicine, but the solution is to some extent in our own hands.

THE PLACEBO.

THE ideal in therapeutics is the employment of a specific remedy for a specific disease, whether such remedy is medicinal, surgical, physical or psychological. Unfortunately there are not enough specifics known as yet, and the therapist must perforce fall back on the help he can give the patient in the circumventing of fate by acquiescence. In this great and true function of the practising doctor the *placebo* has had, and probably still has, a place. It is really surprising to find, on the authority of O. H. Perry Pepper, professor of medicine in the University of Pennsylvania, that the comprehensive subject of the *placebo* is not to be found in the subject indexes of the world literature of medicine.[1] No doubt it has been referred to many times, but no one has ever written about it. What a pity! What a subject for a symposium! Pepper, regretfully noting that even La Wall's survey of two thousand years of pharmacy does not even mention the *placebo*, proceeds to expound the meaning and history of the term. Perhaps in advance it may not be superfluous in these days, barren of Latinity, to point out that *placebo* means "I shall please". The medical profession has inherited the term only fourth hand. The original meaning was words used in vespers in the office for the dead in the Latin service, derived from the 106th Psalm, "*Placebo Domino in regione vivorum*". In the familiar English versions this reads: "I will walk before the Lord in the land of the living." Our author tells that this derives directly from the Hebrew, in which the word *halak* means to walk habitually, and hence to please. Wyclif uses the word *placebo* for the burial service. Very different are the next meanings, as used by Chaucer: as part of a phrase signifying to play the sychophant, and as a name for a flatterer. But let us pass by these rather suggestively sinister meanings and come to the medical use of the word. Pepper is surprised that only as late as 1787 does it emerge in a lexicon, being defined as "a commonplace method of medicine", which, as he dryly remarks, is in one sense only too true. In Hooper's "Medical Dictionary" it appears in its correct medical guise for the first time as "an epithet given to any medicine adopted more to please than to benefit the patient". Incidentally, the word "epithet" is good. The author explains this curious delay in the medical adoption of the word, at least in public, by suggesting that the older physicians' tenacity of faith in their medicines was so great that they would not admit that any were really inactive. We might even suggest ourselves that were a census taken on the value of a number of drugs among doctors, the answers might be strangely varied. Pepper has consulted a number of works on therapeutics and finds that modern authors are more than reticent; as he observes, "they turn up their scientific noses at this humble humbug", apparently regarding the giving of a *placebo* as not mentionable in polite society—one of those things which we all do, but do not talk about. But perhaps this arcane mystery is too much derided. It is not easy to select an appropriate *placebo*. It should be quite inactive for the sake of the patient's safety, and not after the fashion of our more powerful and effective new remedies, sometimes to be feared for the doubtful gifts of other and more dangerous affections that may follow in their train. Further, it must be to some degree impressive. Perry mentions such powerful names as condurango and cimicifuga; but even here we must be careful, for who knows when some clever inquisitive analyst, perhaps wishing to do some original work for a higher degree, may not discover in even the purest herbs of the advertisers some substance with an impressive structural formula and a proven pharmacological action on hamsters or salamanders?

Is the *placebo* necessary? Pepper thinks probably not, provided the patient and his family are sufficiently intelligent; but, as he sadly remarks, few are. Today, with the threat of free medicine over the public's head, there is a new danger: that the incredibly vast consumption of drugs by the people in general will not only be increased, but will include more potent substances than those harmless ones which we have been considering as possibly justifiable in the treatment of those who insist on medicine at any cost. As a profession we should attempt to educate the public, although the way seems hard, long and barren for the educators, who even now cannot really cope with the seductive beckoners along the road. In the dawn of medical history the suppliants at the temples of healing humbled themselves before the gods. They were in the main treated by the primitive dietitians and physiotherapists of the day, and no doubt, in addition to the powerful psychic suggestion which helped to heal them, some simple *placebo* also lent its aid. As human nature has not changed, so far as we can tell, it is probable that even in the mechanical age the same basic factors in healing are necessary, not excluding the harmless *placebo*.

[1] *Transactions and Studies of the College of Physicians of Philadelphia*, June, 1945.

THE PREVENTION OF LEAKAGE AFTER INTESTINAL ANASTOMOSIS.

EVERY surgeon knows, sometimes from sad personal experience, that anastomosis of the colon is always attended by the risk of sepsis following leakage of bowel contents. In order to lessen this risk many procedures have been devised. What promises to be an important advance in this branch of surgery has been recorded in a preliminary report of an experimental study by John Devine.[1] He points out that suturing of the large bowel can be compared with the suturing of the inner tube of a motor car tire. Sutures cannot be used to repair tears in rubber because each stitch would allow the leakage of air to occur; these tears are therefore repaired by the vulcanizing on of patches. The method devised by him consists in the "vulcanizing on" of peritoneal grafts or of split skin grafts over the suture line, whether the surface of the bowel was covered by peritoneum or not. Devine refers to work by Sano, who reported in 1943 a method of "sticking on" skin grafts with dried plasma and leucocyte cream. Young and Favata in 1944 simplified the procedure by using thrombin solution on the unwashed skin graft and normal pooled plasma on the recipient area. Devine's study was undertaken to see whether skin or peritoneum could be grafted over the suture line of colon anastomoses; he recognized that any method which would be successful with the colon would be at least equally successful with the small bowel and stomach. Dogs were used for the experiments. In the first six experiments grafts were applied to the line of the anastomosis without pressure in five instances and with pressure in one. In the case in which pressure was used the animal was killed at the end of a week and the graft was found sticking firmly in position without any sign of leakage or peritonitis. In the five cases in which no pressure was used (the grafts were of skin, peritoneum or omentum), all were firmly stuck, but leakage had occurred at one spot or another. In the case of one animal no graft at all was used and death occurred from fæcal contamination in twenty-four hours. In the second series of four experiments pressure was applied to the grafts; no sutures were used. Two grafts were entirely successful. In one case an extensive hæmorrhage occurred and caused death. In the fourth case a hole was cut in the graft by accident and peritonitis occurred from leakage through this hole. The grafts were stuck on with thrombin and plasma solution. Peritoneal and skin grafts were also applied to an exteriorized human bowel with satisfactory results. A further report on this subject from this investigator will be awaited with interest.

[1] *Surgery, Gynecology and Obstetrics*, April, 1946.

Abstracts from Medical Literature.

PATHOLOGY.

Internal Lesions in Burns.

ROGER DENIO BAKER (*The American Journal of Pathology*, July, 1945) has analysed a series of 96 autopsies in which cutaneous burns or the complications of cutaneous burns were the chief cause of death. The series included 37 cases in which death occurred during the first day, 26 cases with death from the second to sixth day inclusive, and 33 cases with death after the first week. Hepatic necrosis was usually absent, and when present could be explained more reasonably as a result of a complication of the burn, such as infection, than as a direct result of the burn. Necrosis of minimal degree was noted in four cases in which no factor but the burn was demonstrated as a cause. In this series of cases tannic acid treatment had not been used to any appreciable extent. In 28 cases from the period before the use of tannic acid there was no case of hepatic damage due to the direct effect of the burns. It was concluded that the necrosis of the liver is not a lesion characteristic of burns. Karyorrhexis of high degree occurred frequently in the lymph nodules of the spleen in those patients less than seventeen years of age who died during the first three days following burning. Karyorrhexis was absent, or present in minimal degree, in the splenic nodules of those older than seventeen years. Moreover, when those less than seventeen years of age survived more than three days, karyorrhexis was absent or present in minimal degree. While it could not be proved that the striking karyorrhexis present in the young who died during the first three days was not present before burning, it was thought that the karyorrhexis was probably the result of the burn and that it disappeared after the third day because the digestion of the nuclear particles by phagocytic cells rendered them non-stainable with hæmatoxylin. It was concluded that changes in the splenic nodules were not fully characteristic lesions of fatal burns, since these changes were not present in adults. Unequivocal changes in the adrenal and kidney were infrequent. The swelling, congestion and occasional hæmorrhage in the adrenals in early deaths were attributed to shock. Hæmoglobin casts were noted in the kidneys rarely. In general, emphasis is placed upon the paucity of histopathological alterations specific for burns and not attributable to shock, to the rarely occurring hæmoglobinæmia, or to secondary infection.

Primary Intracranial Chorionepithelioma with Metastases to the Lungs.

R. E. STOWELL, E. SACHS AND W. O. RUSSELL (*The American Journal of Pathology*, July, 1945) present the case of a fifteen-year-old boy with a primary chorionepithelioma in the region of the diencephalon with metastases to the lungs. The histological structure of the tumour was typical of chorionepithelioma. Quantitative analyses of hormones showed significant amounts of gonadotropins and œstrogens in the urine, cerebro-spinal fluid and metastatic neoplastic tissue. It is believed that the chorionepithelioma arose in the region of the pineal body from a previously existing teratoma. The testes and other organs were eliminated as sites for a possible primary growth of the tumour by thorough sectioning.

The Vaginal Smear in Diagnosis of Carcinoma of the Uterus.

ACCORDING to Olive Gates and Sheilds Warren (*The American Journal of Pathology*, July, 1945), a total of 341 vaginal smears from 233 women were studied to determine the place of this method in routine diagnosis of the presence or absence of uterine carcinoma. A mistaken positive diagnosis made from a smear should be a problem only in exceptional cases of radiation reaction or of senile atrophy with infection. False negative diagnoses are more difficult to avoid. There are certain types of carcinoma cells which are difficult to recognize without a good deal of experience. Interpretation of smears made after radiation treatment demands more experience than interpretation of other smears because of the changes in epithelium induced by radiation. The smear may be valuable in diagnosis to detect recurrence after radiation, since in these cases biopsy is preferably avoided. As a subsidiary test, the vaginal smear may be especially useful in cases of "hidden carcinoma". This method as a means of final diagnosis has yet to be clearly established. Before this is possible, there must be more specific information upon the limitations and advantages of the method based on larger series of cases. It is the authors' impression that this procedure is promising in a high degree. As a screening test for detecting the existence of cervical or endometrial cancer in large groups of women it may well be of value.

Adenoma of the Bronchus.

ACCORDING to Herman J. Moersch, William S. Tinney and John R. McDonald (*Surgery, Gynecology and Obstetrics*, November, 1945), adenoma of the bronchus is a relatively common tumour involving the tracheo-bronchial tree. It occurs usually among younger persons than does carcinoma of the bronchus, and, in contrast to bronchiogenic carcinoma, is more common among women than among men. It is generally slow growing and usually gives rise to clinical symptoms over a much longer period than carcinoma of the bronchus before the diagnosis is established. In the authors' experience cough is the most frequent and earliest symptom of adenoma of the bronchus. Hæmoptysis, asthmatoid wheeze and recurrent bouts of pulmonary infection are other common symptoms. Adenoma of the bronchus generally presents a characteristic bronchoscopic picture, but the final diagnosis must rest on microscopic examination. Adenoma of the bronchus presents a characteristic microscopic picture. Mitotic figures are usually absent. The type of cell is consistently a fairly small, roundish cell which does not have marked hyperchromatism of the nucleus. The tumour cells consistently make an attempt to form acini, but are rarely very successful in the attempt. A noticeable feature of all adenomata of the bronchus has been their vascularity. In no instance in the authors' series did metastasis occur to the other lung or outside the thoracic cavity. From this study the authors feel that adenoma of the bronchus should be regarded as a neoplasm of the lung *sui generis*. The method of treatment to be employed in cases of adenoma of the bronchus depends on the situation of the tumour, the degree of secondary pulmonary suppuration and the patient's general condition. In their experience endoscopic destruction of the tumour and destruction by surgical extirpation of the tumour by means of lobectomy or pneumonectomy are the most satisfactory methods of treatment.

Solitary Giant Follicular Lymphoma of the Vermiform Appendix.

THREE cases have been described by Robert P. Morehead and W. E. Woodruff (*Archives of Pathology*, July, 1945) in which the appendix was removed following the development of symptoms simulating those of acute appendicitis and in which the appendix showed a localized tumour which was composed of lymphoid tissue. This tumour tissue was characterized by numerical and dimensional hyperplasia of the lymphatic nodules, disruption of follicular outlines and invasion of all coats by large hypochromatic cells, smaller and more chromatic cells and medium-sized lymphocytes. On morphological grounds the tumours observed may be interpreted as examples of giant follicular lymphoma of the appendix with direct transformation into "polymorphous cell sarcoma". At the time of operation each appeared to be a solitary tumour, since the appendix was the only structure found to be involved. In the absence of post-mortem studies, however, opinion must be withheld regarding the solitary nature of these lesions.

Theca-Cell Tumours of the Ovary.

E. A. BANNER AND B. DOCKERTY (*Surgery, Gynecology and Obstetrics*, September, 1945) present data on 23 cases of theca-cell tumour with a correlation of clinical, pathological and chemical data. These tumours appear to be derived from the ovarian mesenchyma and are closely related to the granulosa-cell group of tumours. Occasionally the relation may be a histological one with elements of both types discernible within the same neoplasm. Usually, however, both tumours present "purity" of type. The relatively high incidence, especially in post-menopausal patients, of associated myometrial hypertrophy and uterine fibromyomata, combined frequently with endometrial hyperplasia and cervical and fundal carcinoma, suggests the production by the ovarian tumours of œstrogenic hormone. Inability to demonstrate measurable quantities of this hormone through assays of tumour tissue is perhaps not to be regarded as conclusive evidence of absence of the hormone. A chemical analysis of eight theca-cell tumours gave evidence that these tumours contained increased amounts of cholesterol and cholesterol ester fractions as compared with the values for these substances found present in seven normal ovaries. Although the tumours did not invariably produce clear-cut clinical symptoms, their presence could often be suspected by an alteration in the

menstrual habits of the patient. Post-menopausal bleeding from a hypertrophic endometrium was commonly encountered in these patients. Histologically, in spite of the employment of "new stains", the authors found difficulty in distinguishing certain fatty fibromata from theca-cell tumour. In such doubtful cases examination of the endometrium was often of value.

MORPHOLOGY.

Perception and the Corpus Callosum.

C. S. BRIDGMAN AND K. U. SMITH (*Journal of Comparative Neurology*, August, 1945) investigated a group of patients with surgical section of the *corpus callosum* in order to find the extent to which connexions between the cerebral cortices participate in visual discriminations apparently dependent on integration of function between the two sides of the brain. A general analysis of visual perception in cases of partial and complete sections of the *corpus callosum* disclosed that the following perceptual functions, depending on some degree of bilateral central interaction, were not materially altered by the operations: (*a*) binocular depth perception which involved in part fusion and integration of activity set up by stimulation of the heteronymous hemiretinæ; (*b*) ability to maintain and recover fusion in response to diplopia-producing stimuli; and (*c*) monocular apparent—movement vision involving stimulation of points lying on opposite sides of the vertical mid-line of the eye. However, the data indicate the possibility that the operations produce some deficit in divergence and convergence necessary to maintain and recover single binocular vision. This effect is of questionable significance, and it is clear that these functions are not seriously altered. It is believed that the present experiments offer suggestive evidence toward the view that the subcortical levels of the central visual system serve a prime role in binocular perception and visual fusion independently of bilateral cortical integration. The exact functions of the subcortical optic system in visual depth perception, binocular fusion and movement vision are not directly disclosed by the present data. However, it may be suggested tentatively that the subcortical system, which is known to define primary ocular adjustments, may also provide the means for fusion of binocular images and consequent depth effects in seeing, the pattern and detail of which are refined at the level of the geniculo-striate system.

The Inferior Olivary Nucleus.

W. C. WILSON AND H. W. MAGOUN (*Journal of Comparative Neurology*, August, 1945), in an investigation on cats, add some information to knowledge of olivary connexions. The inferior olive is a conspicuous cell mass and its comparative neurological aspects have been intensively investigated, and although some of its connexions are known, specific evidence for its functional significance has been disappointingly meagre. One or both olives were removed from a number of cats and the animals were decerebrated. Following loss of one olive (with inevitable partial retrograde degeneration of the other), the animals exhibited abnormal movements of the vocal cord, predominantly on the side of the lesion. An intention tremor of the neck muscles was present and some head and body sway occurred on standing. Decomposition of movement, together with hypermetria in the use of the contralateral legs, contributed to ataxia in gait. When tested free, the contralateral legs exhibited an extensor hypertonus occasionally associated with an over-active patellar reflex. As a result of these symptoms, the animals frequently fell to the side of the lesion when standing or walking. With bilateral lesions, laryngeal myoclonus and hypermetria and extensor hypertonus of the extremities were bilaterally present. The characteristic tegmental response to mid-brain stimulation was not altered by loss of one or both olives, nor were inhibitory effects from stimulating the bulbar reticular formation impaired by olivectomy. The absence of one or both olives did not prevent the development of marked decerebrate rigidity. The results emphasize the apparently exclusive relation of the olive to cerebellar function—its loss is followed by cerebellar signs and in its absence the function of other brain stem motor mechanisms is not impaired.

Mechanical Responses of Retina to Light.

S. R. DETWILER (*The American Journal of Anatomy*, July, 1945) gives a review of the literature on retinal photomechanical responses (contraction of cones and migration of pigment in the cells of the pigment layer of the retina) and investigates the role of chemical factors. He also discusses the role of hormonal and nervous influences. Photomicrographs and diagrams are published.

Insertions of Extensor Digitorum Communis.

E. B. KAPLAN (*The Anatomical Record*, July, 1945) dissected the *extensor digitorum communis* in twenty-three fresh and embalmed human cadavers and found that the short insertion into the base of the proximal phalanx occurred in only 38·5% of the 140 fingers examined. Anatomical experiments showed that this insertion, contrary to accepted belief, is not essential functionally. The action of the extensor apparatus and of the intrinsic muscles of the hand was studied both by anatomical experimentation on the cadaver material and by electrical stimulation in more than 100 living subjects. This study emphasized the importance of the connexion between extensor tendon and the capsule of the metacarpo-phalangeal joint in the normal extension of the phalanges.

Sleep Centres in the Cortex.

C. DAVISON AND E. L. DEMUTH (*Archives of Neurology and Psychiatry*, June, 1945) investigated a number of cases of disturbances of sleep. In nine cases they were associated with lesions in the cortex. In none was there invasion of the hypothalamus. In two cases compression of the hypothalamus could not be completely excluded. On microscopic examination, however, there was no evidence of changes in the nerve cells. Increased intracranial pressure was present in only four of the nine cases. It is reasonable to assume that the role played by increased intracranial tension in dysfunction of sleep is negligible, if not totally insignificant. Ocular and endocrine disturbances, except for diplopia in one case and endocrine features in another, were absent from this group of cases. From the study of this series of cortical lesions the authors are of the opinion that some fibres for the control of sleep originate in the cerebral cortex, especially the hippocampal, cingular, frontal, premotor and temporal convolutions. These areas are connected with the hypothalamus by means of the corticohypothalamic pathways. Injury to these areas or to their connexions with the hypothalamus is occasionally the cause of pathologic sleep.

Interosseous Muscles of the Human Foot.

J. T. MANTER (*The Anatomical Record*, October, 1945) has studied the interosseous muscles of 149 feet and observed the following variations: (i) Examples of single heads of origin occurred in each of the dorsal interossei, but were more common in the case of the first and fourth. (ii) The muscles of the second interosseous space varied in the dorsal and plantar extent of their origins. Not uncommonly they displayed an arrangement intermediate between the human and the typical anthropoid pattern, an indication that in man these muscles have experienced a change in origin, rather than a regrouping of their insertions. (iii) A bifid tendon may be encountered in any of the interosseous muscles, but it occurred more often in the second dorsal muscle. (iv) On two occasions the belly of the second dorsal interosseous muscle was doubled. (v) Fusion of the second dorsal and first plantar interosseous occurred twice; it was demonstrated four times by the third dorsal and second plantar muscles. (vi) Two variable slips were present which might be considered to represent the missing interosseous of the plantar series. One is an adjunct of the oblique head of the *adductor hallucis*; the other, a band attaching to the lateral side of the first phalanx of the great toe.

Arteries and Veins of the Lungs.

A. B. APPLETON (*Journal of Anatomy*, July, 1945) examined the arterial and venous pattern of the right upper lobe in a series of fifty lungs with special reference to the distribution of the larger branches seen at the hilum in the broncho-pulmonary segments. The upper division or *truncus superior* of the right pulmonary artery generally divides into two or three branches, namely, the pectoral, apical and recurrent, this last being absent nearly as often as it is present. These arteries and unusual patterns as well as the veins of this region are described and figured.

Two Main Diameters of Female Pelvic Brim.

C. NICHOLSON (*Journal of Anatomy*, July, 1945) reports that pelvimetry by radiology in 640 cases is analysed to show that the length of the conjugate diameter of the female pelvis is very sensitive to nutrition, and that the figures quoted in textbooks of anatomy for this diameter is too low.

Medical Societies.

MELBOURNE PÆDIATRIC SOCIETY.

A MEETING of the Melbourne Pædiatric Society was held at the Children's Hospital, Carlton, Melbourne, on May 8, 1946, DR. A. P. DERHAM, the newly elected President, in the chair.

Gargoylism.

DR. J. W. GRIEVE showed a male child, aged fifteen months, with some of the features of *dysostosis multiplex* or gargoylism. The child had been born at term and the confinement was normal. His birth weight was seven pounds seven ounces. His mother suffered from a twisted ovarian cyst when she was five months pregnant, but this had subsided with the administration of morphine. She had a number of small vaginal hæmorrhages from six months till term. She had suffered from no infectious disease. The baby sucked poorly and breast feeding could not be established. No trouble was experienced with artificial feeding. At first "Lactogen" and later cow's milk mixtures were used.

Dr. Grieve said that he first saw the child when he was seven months old. The mother had observed some stiffness of the legs and hips and had commented on the fact that he had kept his fists clenched. She reported that he had been backward in development and made peculiar snorting noises. At seven months he weighed eighteen pounds six ounces, and his head circumference was eighteen and seven-eighths inches. The forehead was prominent. The breathing was snuffly, though no nasal discharge was present. The features were coarse and he was retarded mentally. There was limitation of movement at the elbows, fingers and knees. The corneæ were not clouded. No localized kyphosis was present and the spleen was not palpable. Dr. Colin Macdonald had reported that the X-ray appearances were consistent with a diagnosis of *dysostosis multiplex*. There was thickening of the frontal bones, the supraorbital ridges being wide and prominent. The calvarium presented a ground glass appearance and the *sella turcica* was small. The ribs were thick and heavy. The vertebræ showed some degree of platyspondylitis, but a hook on the anterior aspect of the twelfth thoracic or first lumbar vertebra could not be demonstrated. X-ray examination of the pelvis revealed bilateral subluxation of the hips and *coxa valga*. The subluxation was poorly defined on each side. The femora were thicker than normal.

Dr. Grieve said that all the stigmata were not present, but sufficient evidence was present to justify his making a definite diagnosis and leaving it in the category of *forme fruste*. A comprehensive article on the subject with good illustrations could be studied in *The Quarterly Journal of Medicine*, 1936.

DR. ROBERT SOUTHBY said that this case was almost a replica of the case he had shown to the society in 1939. Gargoylism was unquestionably an absolute entity, like cretinism, mongolism and achondroplasia. In this case, some of the classical signs were not present, but the patient was only fifteen months old and there was ample time for them to develop. The hands and the general appearance were characteristic. Dr. Southby said that the child he had presented also had congenital dislocation of the hips; his brother, also a gargoyle, had the same abnormality. The hips became more and more flexed as the children grew older and both had succumbed to bronchopneumonia.

Tumour of Bone.

DR. JOHN COLQUHOUN showed a male child, aged ten years, with a tumour of his right femur. One month previously, after kicking a football, the child felt a stinging pain in the middle section of the right thigh anteriorly. The pain lasted a few minutes. The child had to cease playing after he made several attempts to resume the game. The pain occurred intermittently thereafter and lasted for minutes or hours and interfered with sleep. On examination the boy was pale and presented a diffuse swelling of the right thigh anteriorly in the middle third. This swelling appeared to extend about four inches in the long axis of the limb and about two inches transversely. The knee and hip region apeared normal, but the adductor muscles on the right side showed evidence of spasm. Flexion of the knee was limited beyond 90° by pain in the area of the swelling, but to this point was free and painless. On palpation there was exquisite tenderness over the swelling, especially at its proximal and distal limits and over its centre. The swelling was firm, but not hard. It was not fluctuant at any point. The inguinal glands were enlarged on both sides, but these were not tender or inflamed. The circumference of the right thigh six inches above the mid-patellar line was half an inch greater than the corresponding area of the left side. No abnormality was discovered on examination of the abdomen or the remainder of the body. The child's temperature was 101·8° F. when he was first seen, but during his stay in hospital it was usually sub-normal and never rose above 99·4° F. The Wassermann test produced no reaction. The blood sedimentation rate was twenty millimetres per hour. The result of the Mantoux test was negative. The red cells numbered 4,500,000 per cubic millimetre. There were 15,200 white cells per cubic millimetre, and of these the polymorphonuclear cells numbered 56%, the lymphocytes 28% and the monocytes 5%. X-ray films had been taken at intervals. These showed irregular periosteal reaction and spotty absorption of the cortex in the middle section of the shaft of the lateral part of the right femur. No metastases could be seen in an X-ray photograph of the chest.

Dr. Colquhoun said that Ewing's tumour appeared to have an affinity for the long bones, particularly the upper third of the femoral shaft. There was frequently a history of trauma. Such tumours presented clinical signs of inflammation, such as periodic bouts of increased temperature, pain and local tenderness, but relatively little increase in the girth of the limb at the site of the tumour. The radiographs showed an increase in the width of the medullary cavity of the involved bone, coarseness, and later destruction of much of the cancellous bone and a gradual expansion of the shaft. Periosteal new bone was deposited in layers which might be clearly defined at the periphery. So diffuse was the margin between the normal and the tumour tissue that the limits of the latter could not be defined. Faint ill-defined shadows of calcium deposits might be seen in the soft tissues adjacent to the bone.

DR. KAYE SCOTT discussed the matter of diagnosis. He said that the history of injury was not characteristic; it was a history of pain while playing football. Injury was often a real prelude to osteogenic sarcoma, but not Ewing's tumour. Also, the occurrence of pain usually preceded the local swelling; the reverse occurred with an osteogenic tumour. The temperature was more characteristic of Ewing's disease, this and other features sometimes simulating acute osteomyelitis. The radiological appearances in the early films suggested Ewing's tumour rather than osteogenic sarcoma, as the situation was in the centre of the shaft, a considerable length of bone was affected and changes involved cortex and medulla, with destruction of both. Furthermore, there was evidence of some endosteal reaction and subperiosteal tumefaction and reaction. As shown in the later film, the amount of subperiosteal bone proliferation was in excess of anything that had been seen previously in Ewing's tumour and seemed to necessitate a radiological diagnosis of osteogenic sarcoma in spite of the other findings. The discrete rounded patches of calcification lying beyond the periosteum could not be readily accounted for. Dr. Kaye Scott then suggested that estimation of serum alkaline phosphatase content would help—this was raised in osteogenic sarcoma, but normal in Ewing's tumour. The next step was an aspiration biopsy. This procedure did not open up tissue planes as would a surgical incision and risks of fungation were avoided. However, only small amounts of tissue could be obtained, but usually sufficient for the necessary diagnosis. If this failed, a therapeutic test of radiation should be given, Ewing's tumour being remarkably sensitive in contrast to the osteogenic sarcoma. Only as a last resort should surgical incision be made into a tumour likely to be osteogenic, so great was the risk of fungation.

A definite diagnosis was needed as radiation techniques were essentially different for the two conditions. Ewing's tumour had been variously regarded as a round-celled sarcoma, a perivascular endothelioma, a reticular-celled sarcoma, while Willis, when in Melbourne, had shown that a primary neuroblastoma in ganglionic tissue resulted in bone metastases which appeared as Ewing's tumours. Dr. Kaye Scott mentioned that in the last two cases in patients under his care, primary neurogenic tumours were responsible. One case came to autopsy at the Austin Hospital, and macroscopic examination of the adrenals showed nothing abnormal, whereas histological examination revealed a very small primary adrenal neuroblastoma. In the other case there were present bone secondaries which exactly reproduced a classical Ewing's syndrome, secondary to a retinoblastoma in an infant. Thus in all cases the radiotherapist

was bound to treat the area between the first lumbar and the second sacral segments in which Willis had found most primary tumours, as well as the bony lesions.

Dr. Kaye Scott, in discussing radiosensitivity of Ewing's tumour, pointed out that in every cell population variability of sensitivity of individual cells was present, and while in Ewing's tumour the majority of the cells were extremely sensitive, a resistant proportion persisted. Even after heavy radiation autopsy specimens showed residual neoplastic cells, and while the main mass of the tumour disappeared and regeneration occurred, local recurrence was the rule unless repeated doses were given. Invariably death occurred as a result of multiple bone metastases, with skull secondaries usually a prominent terminal feature. The radiation technique used in Ewing's tumour depended on these facts. A short intensive course was administered to the initial bone manifestation, and was repeated at intervals. As soon as possible the paralumbar areas were treated against a possible primary growth, and other bone metastases were radiated according to indication. In the presence of terminal cachexia, radiation therapy was used only to control pain or sites of possible fungation.

The treatment regimen that Dr. Kaye Scott favoured for osteogenic sarcoma depended upon the relative non-sensitivity of the group of connective tissues and upon the factors of rapid dissemination by blood stream of tumours arising from them. Epithelial tissues were more radiosensitive than connective tissues. This "tissue sensitivity" depended upon the capacity of cells of the tissue to reproduce themselves under varying conditions. Radiation dosage could be administered to certain epithelial tumours with destruction of the component cells and without damage to the stroma, but dosage sufficient to cause similar death of tumour cells in a sarcoma of bone or connective tissue would result in massive necrosis. It was known that the sensitivity of tumour cells in mitotic phases was greater than that of the resting tumour cells. Stebbins, of London, suggested that small doses of radiation administered to such tumours over a prolonged period might produce results, and by the use of such dosage methods with overall treatment times prolonged to ten weeks, diminution of tumour and regeneration of destroyed bone often occurred. Such courses were then repeated at intervals.

Dr. Kaye Scott said that among his early cases in which patients were treated along such lines, two had survived, to show recurrences at four and a half years and seven years; one, still well, had remained symptom-free for seven years. He did not believe that even this radiation technique was adequate to kill all the tumour cells and considered that amputation should follow the radiation at the appropriate time. All surgeons were depressed by the inevitable mortality following immediate amputation. Dr. Kaye Scott considered that any damage to tissues liberated growth-promoting substances which stimulated normal healing processes. Following a large operation it was probable that circulation of such substances stimulated into active growth any metastatic tumour cells in distant sites. He drew attention to the frequency with which enlarged supraclavicular glands were found immediately following operation for carcinoma of the breast—it could not be imagined that these had been missed in the preliminary examination. The only explanation was fulmination in the post-operative convalescent stage of microscopic deposits in glands not then clinically enlarged. Dr. C. H. Kellaway had demonstrated growth-promoting substances of tissue origin in work done before he left Melbourne. However, the body had defence mechanisms against deposited tumour cells and it was probable that but few of the malignant emboli which reached the pulmonary capillary bed ever survived. But the lungs could not stand up to continuous flooding with metastatic cells without the development of some secondary deposits.

Dr. Kaye Scott thought that probably radiation of the bone primary caused early inactivation of the tumour with less tendency for blood-borne metastasis to occur. If such was the case the lungs had better opportunity of dealing with any tumour cells already deposited, especially if the patient's general condition was improved simultaneously as a result of appropriate medical and dietetic treatment. He quoted the experiments in which implanted mammary carcinomata in mice were treated with vigorous massage. Mice killed some hours later showed very many carcinoma cells in the pulmonary capillary bed, but control mice killed some weeks later showed but few surviving pulmonary metastases, indicating the capacity of the lungs to deal with the foreign cells.

Application of these facts to the treatment of osteogenic sarcoma indicated that the primary treatment should be prolonged courses of radiation to the primary site over a period of twelve to eighteen months. During this time every effort should be made to improve the patient's general condition so that he was offered the maximum chance of overcoming his own pulmonary secondaries; and on this fact treatment availed or failed. After eighteen months, in the absence of secondaries, or earlier if radiation was failing to control the primary growth, amputation should be undertaken. Dr. Kaye Scott said that radiation failed to control the primary osteogenic sarcoma in a minor proportion of the cases, that pulmonary deposits appeared immediately in others, but that in some cases the appearance of secondaries seemed to have been delayed. In only a small proportion had total success been obtained, and in some of these amputation had not been possible on account of the site. Osteogenic sarcoma in a child was still a very fatal disease.

DR. J. G. WHITAKER thanked Dr. Scott for his illuminating remarks. He asked, if a negative result was obtained by aspiration of the tumour, whether incision and biopsy would be considered before radiotherapy was used. Dr. Scott replied that there was not the same risk of biopsy in Ewing's as in osteogenic sarcoma, as immediate X-ray therapy would prevent fungation in the former condition. The natural protective barriers of the expanded tissue planes should be preserved in osteogenic sarcoma—incision undoubtedly stimulated growth and fungation was a dreaded but frequent complication. If biopsy was essential the aspiration biopsy needle should be used. A large bore blood transfusion needle with the centre coned out forming sharp edges to the needle bevel was used. It was connected to a twenty-millilitre syringe to give heavy suction. Satisfactory quantities of tissue for histological examination usually could be obtained without excessive trauma or tissue damage. Experience had proved that the aspiration biopsy needle was an invaluable aid in the accurate diagnosis of suspected tumour. Incision for biopsy should be carried out only as a last resort when osteogenic sarcoma was suspected.

Dr. Colquhoun, in reply, referred to an experience he had had as a house surgeon. A child had a tumour of the ilium which was cut down upon. The surgeon made a tentative diagnosis of osteomyelitis, but sent a specimen for biopsy. Professor Wollbach reported chronic inflammatory tissue. However, the wound fungated and the child succumbed. At post-mortem examination another pathologist after an intensive search found two tumour cells in a large mass of tissue. It therefore seemed that there was quite a chance that it would not be possible to make a diagnosis by biopsy. The evidence favoured Ewing's tumour and he felt inclined to submit the child to radiotherapy.

(To be continued.)

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 105, of June 6, 1946.

ROYAL AUSTRALIAN AIR FORCE.

Citizen Air Force: Medical Branch.

The appointments of the following officers are terminated on demobilization with effect from the dates indicated: Temporary Squadron Leader C. B. Hudson (263255), 15th March, 1946, (Temporary Flight Lieutenants) N. G. Dobell-Brown (267113), 11th March, 1946, C. R. Watson (266788), 14th March, 1946, G. B. Goswell (267238), 15th March, 1946.

Reserve: Medical Branch.

William Peter Harvey Dakin (261274) is appointed to a commission with the temporary rank of Squadron Leader with effect from 5th December, 1945.—(Ex. Min. No. 156—Approved 29th May, 1946.)

CASUALTIES.

ACCORDING to the casualty lists received on June 12, 1946, Captain E. C. Eagleton, Nedlands, Western Australia, is reported as having died of illness.

Correspondence.

SPINAL ANÆSTHESIA AND CHLOROFORM: A COMPARISON OF MORTALITY.

SIR: I was not surprised to read the letters commenting on my recent paper of April 20 on comparative mortality statistics of spinal anæsthesia and chloroform. I have read the same sort of thing in back numbers of *The Lancet* of 1878, resenting Lister's new surgery. People do not like questioners, sceptics, and inconvenient disturbers of their minds, not even when they are right. Sacrilege is unpardonable. The same sort of thing can be noted in back numbers of *The Lancet* and *British Medical Journal* of 1890 and around that time, when the chloroform men were angrily throwing what bricks they could against the statistics (very awkward statistics) shown by the advocates of ether. Those statistics were greatly disliked. Men were told they did not mean what they seemed to mean; and so on.

Your correspondent Dr. J. E. M. Thomas is well in line with the older reactionaries. He tells us (wisely) that he has no intention of entering into pros and cons, but writes "to protest against the uncritical use of data in this so-called statistical study". He does not like the data. However, I did not make them. People died. That was how the data were made. People will continue to die, just like the others, unless we find some way of effecting an improvement. That is the reason for "so-called statistical study". A worth-while study, or so I think.

Then, "with a disregard for space and time which even Einstein might envy", I am said to do various things and, having done them, to present "a figure purporting to show that spinal anæsthesia is much more dangerous than chloroform anæsthesia of fifty years ago". Did I? After all, here is what I really did say, and this time I will put some of it in italics, so that there can be no more perversion. "*If the statistics are soundly based*, the chloroform anæsthesia of fifty years ago was at the least twice as safe as the spinal anæsthesia of today." (Your correspondent Dr. Marshall thinks I should have said "fifteen years ago", instead of "today".) However, it seems that Dr. Thomas is angry because I have brought the matter up at all. For he cannot but agree with what I really did say, as just quoted, and it would have been much better if he had quoted correctly. He may not think the statistics are correct. He may wish them to be incorrect. But as I have said, I did not invent them, and, correct or incorrect, why hide them from inspection? Dr. Thomas tells us that the material should have been left "decently buried". Well, it was not. Dr. Thomas's method of deciding questions has always had many followers. What about the patients who might also be buried, decently perhaps, but who might otherwise have lived? These are serious matters that we are discussing.

In the third paragraph of his letter, Dr. Thomas charges to me "the fallacy of the assumption that every death on the operating table is to be attributed to the anæsthesia". That is one of Dr. Thomas's methods of controversy, and it does him no credit. Let your readers turn to the latter part of my article where I make the remark: "They may be inclined to say that it is not spinal anæsthesia that causes the deaths, but its practitioners. They are certain to be at least partly right—but it would appear from Babcock's experience that skill is not everything."

In his fourth paragraph I found Dr. Thomas still not particular as to accuracy. Why swell 20,012 cases so carelessly up to 50,000?

Dr. Thomas spends some effort on presenting a view that spinal anæsthesia patients of today are worse risks than the chloroform patients of fifty years ago, because at that time the scope of surgery was smaller, and his suggestion is that it made the risk smaller, so that "to compare the patients of the chloroform era with those of today is completely unjustifiable".

As for the difference in risks, there have always been bad risks. If we can say anything, I think we can say that, on the whole, the risks are much better than they were fifty years ago; not worse, as Dr. Thomas suggests. At that time comparatively few patients were operated on while they were in a good condition. Operations were much more dangerous, and people had often good reason to doubt whether an operation might not be worse than the risk of the disease. Operations were postponed until the patient was very ill. They were operated on when it became obvious that there was little chance without it. And then they had an anæsthetic. On this came controversy. Ether had begun to compete with chloroform. Mortality records were compared. Some of the chloroform figures were those I quoted in my article as showing up so much better than the spinal cases, as far as over-all statistics were concerned. And yet those chloroform records were considered a reproach, as compared with ether, which means, of course, the ether results of those days.

And then came the Second Hyderabad Commission, with Surgeon-Major Lawrie as President, and Sir Lauder Brunton, F.R.S., as one of its members. This commission ended its report[1] by saying that if the method they described were carefully used, there would be no deaths from chloroform, "which could be given with perfect ease and perfect safety". Any deaths that occurred would therefore be due solely to the fault of the practitioner, not to chloroform as an anæsthetic. Lawrie pushed these opinions very vigorously in *The Lancet* and in the *British Medical Journal*. In an article in the *British Medical Journal*[2] he said that "no anæsthetic is absolutely safe except chloroform administered on Syme's principles". In the same article, he expressed the opinion that the publication of Julliard's[3] figures of 524,507 cases of chloroform anæsthesia with 161 deaths, or 1 in 3,258, and Roger Williams's[4] list of 12,368 with 10 deaths, or 1 in 1,236 (appearing in my article as quoted by Waller), were "intended to show the danger of chloroform", though in my article they would be used to show the relative safety of chloroform. Lawrie had to admit that there were deaths, but in his view they were all, without exception, the fault of the practitioner. In a clinical lecture published in *The Lancet*[5] he put forth a series of 45,000 cases of chloroform anæsthesia, extending over forty years, without a death.

Lawrie has passed on, but his spirit survives. Reincarnated, it has taken up spinal anæsthesia, and speaks through your correspondents, who tell us that if deaths occur, it is the fault of the practitioners, or, as Dr. Marshall would say, because they still persist in using the methods of fifteen years ago, which produced the death rate recorded in 1932.

But what is this new technique that has made that of fifteen years ago obsolete? I have mentioned Ansbro and Pico.[6] They claimed that the technique described in their article of 1942 as "continuous spinal anæsthesia" made spinal anæsthesia newly safe. They did not prove it, but they said it was so, and they contributed 100 cases without a death in support of it. They then set about contrasting the new method with what they alleged was the great mortality of "single dose" technique, and they quoted Babcock's 15,652 cases with a mortality of 1 in 391 as going to prove it. They quoted other results which they represented as much worse than Babcock's statistics, for example, a shocking mortality rate from the Toronto General Hospital. As to that, I have received a private letter from Dr. Shields, chief anæsthetist of the hospital, which shows the figures to be completely false, and wholly and entirely a fabrication.

Now, is this the modern technique that your two correspondents—my critics—say has superseded that of not so long ago? Is it what they practise? Or are they still "single dose" spinal anæsthetists, to be placed by Ansbro and Pico amongst the back numbers of fifteen years ago?

There is more to be said than that. We are told, on "I say so" authority, not to admit certain serious scientific work that I have made use of. Is it because it discovers something that your correspondents would keep hidden? As far as I know, these are the only researches of the kind that have ever been published. They remain in the literature to this day what they were then, the only source from which we can get uncoloured over-all figures. We can get statistics from particular men or groups of men. They are useful and interesting. But we want also something that is as nearly as possible a census of all cases, all results, all administrants. That is what an insurance office would want to know. But it is not the information that comes from Thomases and Marshalls, or from anybody who would be willing to see some of the truth "decently buried". There is a lot of burying done, as happened years ago in one of our hospitals when in one week there were three deaths from a certain anæsthetic. The journals get the favourable notices, not the whole facts.

In the concluding part of my paper, I put in, for the benefit of spinal anæsthesia, 11,000 cases assumed to be completed without a single death, whereas there had been already 20,012 with 56 deaths. These 11,000 were, by convention, distributed to eleven men who had an experience of 1,000 cases in ten years without a single death. I remarked that "at the end of the period there would be a number of men who could get up at a medical meeting and tell about their success, or perhaps they would write about it. They are likely to feel pretty sure about their skill, and rightly so. They may also feel that it will not happen to

them to have deaths, such as others have had. They may be inclined to say that it is not spinal anæsthesia that causes the deaths, but its practitioners", and so on. I had previously warned against picking out individual experiences, even our own, and using them as representative of all, since that would involve the fallacy of arguing from the particular to the general.

Well, it has come about as I prophesied. Here are two of our eleven. We are told that it is the so-much-improved technique that is used, or not used, that makes all the difference. It is what the practitioner does, or fails to do. That is all. And that is the Hyderabad Commission and Surgeon-Major Lawrie over again.

Then, as to arguing from the particular to the general. Dr. Marshall tosses all that aside. He insists that "local figures or opinions" would have afforded me "valuable enlightenment".

Opinions! Enlightenment! I want the whole truth. So would intelligent patients. So would insurance companies, if they were interested. So would many readers of this journal, who have to make up their minds on behalf of their patients in these grave matters.

Yours, etc.,

C. E. CORLETTE.

Sydney,
May 30, 1946.

References.

(1) "Report of Second Hyderabad Chloroform Commission", *The Lancet*, Volume I, January 18, 1890, page 149.
(2) E. Lawrie: "Chloroform or Ether?", *British Medical Journal*, Volume I, June 13, 1891, page 1380.
(3) Julliard: Quoted in leading article, "Ether or Chloroform", *British Medical Journal*, Volume I, April 25, 1891, page 920.
(4) Letter in *The Lancet*, Volume I, February 8, 1890, page 317.
(5) E. Lawrie: "Clinical Lecture on the Hyderabad Chloroform Commission *et cetera*", *The Lancet*, Volume II, November 29, 1890, page 1143.
(6) F. P. Ansbro and L. J. Pico: "Continuous Spinal Anæsthesia: Report of 100 Cases in which this Method was Employed", *The American Journal of Surgery*, New Series, Volume LV, March, 1942, page 504.

THE NATIONAL HEALTH SERVICE BILL OF GREAT BRITAIN.

SIR: In the editorial of THE MEDICAL JOURNAL OF AUSTRALIA of April 13, 1946, was published the criticism of the British health plan drawn up by the British Medical Association.

Four main principles were stated which form the basis of opposition to the plan and which require further discussion in relation to the plan.

Principle I: It is misleading to claim this principle on behalf of the medical profession as a whole, in view of the fact that the referendum among the British practitioners revealed a willingness among a large proportion to serve in a salaried scheme. However, this principle implies that the acceptance of a salaried medical service is not "in the public interest" and that the profession will thereby become less efficient and less sincere.

At present the poor and middle classes do not have a complete health service; only the wealthy are able to avail themselves of every facility.

Any attempt to provide a complete service for all is obviously in the public interest.

Political and social trends indicate that sooner or later the medical profession must become a salaried service. It has been said that there are too many young men and women entering the profession; yet it is common knowledge that the wealthier residential areas at present are served by a far larger number of doctors than the poorer ones. A properly organized salaried medical service will require a greater number of doctors than at present to provide adequate services everywhere. This in turn will call for far more students not only in medicine, but in dentistry and other professions.

Principle IV: Like all other workers, doctors have a very limited choice in the form, place and type of work, their desires being governed by outside, mainly economic, conditions. Only a few with adequate resources can follow a predetermined career. Opportunities for medical education and specialization will be much greater under the salaried medical scheme than at present.

Principles V and VII are acceptable to everyone. The profession must insist that any qualified and registered practitioner has a right to practise in any government medical service; but it is difficult to understand the inclusion of these two principles in view of the fact that Council apparently intends to recommend the non-acceptance of the scheme as a whole.

I would submit two criteria which I consider should form the basis on which the efficiency of any service should be judged: (1) Every citizen has a right to free medical service from birth to death—service being regarded as fulfilling every requirement for the maintenance of health and treatment of disease. (2) It is the right of every citizen to receive from the State an education, free and adequate to fit him for the vocation of his choice.

The present form of medical practice requires, therefore, considerable alteration. Fellow members might well devote more time to social problems both as they relate to the profession and generally.

Any plan to be of greatest benefit to both patients and profession must be drawn up by the profession itself. How otherwise can we ensure that it does not include any undesirable features? Such a move has already begun. Many local associations are of the opinion that the question of a salaried medical service should be discussed, and in 1944 the Warringah Association actually drew up plans for such a service.

As a salaried medical service would be a progressive and beneficial step, the councils of the British Medical Association should reconsider their present official attitude and really become front-rank champions of progress in health matters.

Yours, etc.,

STEFANIA SIEDLECKY.

The Rachel Forster Hospital,
Redfern,
New South Wales.
May 30, 1946.

THE PHARMACEUTICAL BENEFITS ACT, 1945.

SIR: Concerning the following reply to Dr. F. W. Simpson's statements about me in your journal of September 15, 1945, I wish to point out that the chief cause of delay in my response has been ill health.

As far back as October, 1945, I had asked for relief on this ground; unfortunately this was not possible, and in January, 1946, my health broke down completely and I had to commence an extended rest immediately.

Dr. Simpson accused me of "bitterly slating the British Medical Association" in the *West Australian*. This is not true. Readers will please note:

1. If I wanted to attack the Association, I would name it.
2. The Association was not mentioned in the letter referred to.
3. The Association's objection to the "personal examination" clause in the act was publicly championed by me in it. This is what Dr. Simpson calls "bitterly slating the Association".

The attack on the act was originated from well-known non-medical sources and was supported with much free space by the daily Press. I "bitterly slated" these groups and their virulent hostility to improved social services.

It might be said that this letter was an indirect attack on the Association; I can only say that such an idea is merely an inferential assumption based on a situation I did not help to create, as I have never attempted to involve the Association in the political campaigns of the aforementioned groups and their Press.

Yours, etc.,

LESLIE R. JURY.

38, Strickland Street,
South Perth,
May 20, 1946.

PLACENTA PRÆVIA.

SIR: I was pleased to see that I did get a reply from Professor Bruce Mayes to my letter in THE MEDICAL JOURNAL OF AUSTRALIA of April 6, 1946.

Firstly, the annual hospital report of the Glasgow Royal Maternity and Women's Hospital for 1937 shows that from 4,724 admissions, ante-partum hæmorrhage was present in 305 cases. Two hundred and twenty-four Cæsarean sections were done from all obstetric abnormalities. Dr. Hart was registrar in that hospital from 1929 to 1933, during which time he must have been responsible for the admission and supervision of 1,200 cases of ante-partum hæmorrhage.

Professor Munro Kerr, retired from active practice in 1929, quotes shock, hæmorrhage, and collapse accounted for 70% and sepsis for 30% of deaths during his time at the Glasgow Maternity Hospital (*The Journal of Obstetrics and Gynæcology of the British Empire*, June, 1939, page 535).

From the above statistics it is obvious that the majority of the deaths could have been prevented by an early diagnosis in doubtful cases by the examination without a glove

when the patient is in good condition with a mortality rate of less than 1%. Mortality rates in the region of 10%, as quoted in Dr. Syred's paper, could easily be reduced to less than 1% by the employment of procedures which have been in vogue in Glasgow for ten years.

Secondly, I agree that Cæsarean section under general anæsthesia is a serious operation and will never be done by me again after having found the simplicity of a local anæsthetic. During the past three years I have done fourteen Cæsarean sections under local anæsthesia, and the nurses find that the patients have no more discomfort than those having had an appendix removed. Previous to that I did one operation under general anæsthesia in which the patient nearly bled to death and cured me for all time of this form of delivery.

Yours, etc.,

J. N. R. STEPHEN.

Stockton,
New South Wales,
May 27, 1946.

HONORARY MEDICAL STAFFS.

SIR: The Council has recently published in the monthly notices the following resolution:

> That the Council is of the opinion that a vacancy on the senior honorary staff of a public hospital should be filled by the candidate already on the honorary staff and next in line of succession, provided that he has carried out his duties efficiently and to the satisfaction of the board of the hospital. . . .

I wish to place on record my emphatic disagreement. I consider the resolution is not in the best interests of either public or profession.

In the first place, it seems to me to negative that very principle of free competition so generally acclaimed of late. The man on the spot who has served the hospital long and well should have already a sufficient advantage over his competitors; also, the public should be able to get the best man available.

The system advocated by Council means:

1. That if two men are equally qualified for a hospital appointment, the one who travels abroad for a number of years is that much junior to his colleague on his return.
2. That the capable country surgeon who finally comes to Sydney, perhaps because his children have grown up, has only one place—the bottom. He has not the chance to place his qualifications fairly in the scale against the city man who is already on the staff.
3. That there is still only one place—the bottom—for the experienced man from another country or State who desires to settle in Sydney and take up a public hospital appointment. Doubtless, leave for an honorary here would be granted for one or two years for study abroad, but should he wish to spend five years or even be uncertain of his return at all, and finally come back—a vastly improved man—would not he have to climb the ladder all over again, if he were not considered too old?
4. That once on the staff, there is no need to improve; it is enough to do one's routine duties and wait for promotion.

Yours, etc.,

C. C. MCKELLAR.

"Harley",
143, Macquarie Street,
Sydney.
June 7, 1946.

RESEARCH AT THE KANEMATSU INSTITUTE.

SIR: The expressed anxiety of the Board of Directors of Sydney Hospital to reopen the research section of the Kanematsu Institute is in contrast to the haste and secrecy with which the decision to suspend research was made by the Board before the possibility of the decision becoming a matter of public interest was apparent.

The explanation made by the Board in justification of its action is based on two major points: lack of funds and the disintegration of Dr. Eccles's research team.

It was to be expected that after the resignation of Dr. Eccles his collaborators in neurophysiological investigation would move to laboratories where they could work once more in association with masters in their chosen field.

It is not customary for research institutes to suspend activities because of the dispersal of one research group. Rather is it the practice of competent administrators anxious to foster research to maintain a continuity of investigational endeavour by building new teams of workers around any nucleus of research in being. In all research institutes workers come and go; such interchange is favoured and encouraged by those knowing something of the needs of research and of research workers. This is probably the only occasion on which such a natural process as the dispersal of a research team has been seriously adduced as a reason for closing a laboratory in which active research was still in progress.

The Board of Directors has stated in the lay Press that research at the Kanematsu Institute was "virtually at a standstill". If such were the case, why did the Board sanction the expenditure of £4,933, which included grants of £645 from the National Health and Medical Research Council, on such research during 1945? The research on which this amount was spent with the full knowledge of the Board was, with the exception of that in the hands of Dr. Kuffler, still in progress and giving promise of further development when the Board's instruction to suspend all research on April 1 was transmitted to me on March 1.

With what knowledge or on what well-informed advice was this decision to suspend activities reached? No member of the Board ever took the trouble to inquire what research was in train or what was contemplated. In a letter from the secretary of the hospital to the acting director, written towards the end of 1945 and conveying a ruling of the Board on the functions of the Kanematsu Advisory Committee, it was stated that this committee was to advise the Board on matters of scientific importance. This committee was not consulted on the question of suspending research; on the contrary it was abolished on April 1. It would seem that the Board did not consider the suspension of research a matter of scientific importance. The Board did not inquire from any competent authority what work would be interrupted by the implementing of its decision, what the remote effects of the decision might be, or whether any alternative suggestions could be made; suggestions which might have spared the Board its present anxiety to reopen an institute which should never have been closed.

It has not been revealed by the Board that early this year Dr. F. B. Byrom, post-graduate lecturer in pathology in the University of Sydney, was refused permission to work for a short time in the institute by the House Committee of the Board on the grounds that there was no accommodation for him. Yet I, as acting director, had informed the president of the Board that ample accommodation was available. Dr. Byrom's work was to be financed from extraneous sources and would not have called for any support from Kanematsu funds. Did this refusal to help a research worker of the status of Dr. Byrom betoken anxiety to foster research?

During the past two years several research workers, some of senior status, sought to join the research staff of the institute, and there is no reason to suppose that, had encouragement been offered, recruits would have been lacking after April 1, 1946.

Much is made of the "temporary" nature of the suspension of research. Why should a temporary suspension call for the abolition of the Kanematsu Advisory Committee? Would not a board anxious to promote research have consulted the committee as to how research might be maintained most effectively in the face of any obstacles and on ways and means of obtaining additional financial support—from private sources, for example—while the accumulated subsidies were being spent as the Hospitals Commission had directed?

It was from the annual subsidies paid by the Hospitals Commission that the bulk of the £8,000 capitalized by the Board was derived. When the president of the Board of Sydney Hospital, who was also chairman of the Kanematsu Advisory Committee, was vice-chairman of the Hospitals Commission, certain members of that commission had already raised the question of suspending the annual grant to the Kanematsu Institute because of the amounts that had been accumulated from these grants. Soon after the commission was reconstituted late in 1944 the subsidy was in fact suspended. When two deputations from Sydney Hospital discussed Kanematsu Institute finances with the Minister for Health last year, the discussions were based on the assumption that the £8,000 now said to represent an endowment fund was available for use as liquid assets. It was never claimed on behalf of the hospital that only some £2,000 or £3,000 was at its disposal for the prosecution of research. Yet this, if a valid claim, would have strengthened greatly the hospital's request for a continuance of the annual subsidy.

The Board's statement reveals that from July 1, 1945, the cost of research has been £2,700. Assuming that the same rate of expenditure—£3,600 *per annum*—were maintained, a

simple calculation will show that, with interest at 3% on residual funds, the £8,300 still available for use as liquid assets would, apart from any special grants, suffice for nearly three years; not for "about eighteen months only". There would still remain £8,000 unquestioned endowment.

If the Board considered that it had a legal right to "create" an endowment fund from accumulated subsidies, then it was, on April 1, legally competent as well as morally bound to reconvert these moneys to liquid assets to be used for the maintenance of research in being. Instead it wantonly betrayed a trust which it assumed when it originally called the research unit into being and, ignoring a written protest from me which incorporated a plan for the continuation of research with a minimal expenditure, struck at the very basis of security in research careers by destroying the research activities of one of the all too few centres of medical investigation in the Commonwealth.

The Board ends its statement by the publication of certain selected letters. I suggest that in the interests of truth it publishes all the correspondence between the Board and the Hospitals Commission and between the Board and myself which relates to the events leading to the suspension of research activities, to my rejection of the offer of the directorship of the emasculated institute and resignation from the staff of the hospital, and to events subsequent to my resignation.

Yours, etc.,

A. J. CANNY.

16, David Street,
Clifton Gardens,
New South Wales.
June 10, 1946.

TRIGEMINAL NEURALGIA.

SIR: It can surely serve no good purpose to publish the isolated experience of one individual as a condemnation of a universally accepted form of treatment.

The portion of the correspondence of Dr. Alec Lyons (THE MEDICAL JOURNAL OF AUSTRALIA, May 25, 1946) to which I take exception is as follows: "I can state that interference with the sensory root of the fifth cranial nerve is worse than useless."

Yet, perhaps, there is truth in the above statement. "Interference" with any structure is, to say the least of it, undesirable. However, clean-cut surgical division of the fifth nerve root has, does and always will relieve trigeminal neuralgia except in the cases of those unfortunates whose nervous stability has been ruined by a multiplicity of unsuccessful treatments and those in which an irremovable tumour is the cause of pain.

Yours, etc.,

F. J. CLARK.

194, St. George's Terrace,
Perth,
June 5, 1946.

University Intelligence.

THE UNIVERSITY OF MELBOURNE.

NUFFIELD MEDICAL ENDOWMENT.

THE University of Melbourne has the right under Lord Nuffield's scheme for the endowment of demonstratorships and clinical assistantships for dominion university graduates at Oxford University Medical School to nominate one of the following for appointment in October, 1946: (a) a demonstrator in biochemistry, (b) a demonstrator in pharmacology, (c) a clinical assistant in surgery, (d) a demonstrator in physiology.

Members of the staff or graduates of the University who wish to be nominated are invited to apply to the Registrar of the University of Melbourne before July 6, 1946.

To be eligible for nomination, the candidate must (i) hold a medical qualification by virtue of his being a medical graduate of a university in Australia, New Zealand or South Africa; (ii) have had experience in research; (iii) intend to return on termination of his appointment to Australia for at least five years' work of a like nature to that carried out during the appointment.

The appointment is for three years, and the emoluments are £400 sterling *per annum* in the case of a woman or of an unmarried man, and £600 sterling *per annum* in the case of a married man, payable quarterly in advance, save that the last such instalment is payable in arrear and only on return to Australia or New Zealand. The sum of £150 is also provided for travelling expenses, one-half to be paid on appointment and the remaining half on termination of the appointment. A person appointed will not be permitted to enter for any professional examination except with the consent of the head of his department.

Post-Graduate Work.

COURSE IN CLINICAL PATHOLOGY AT SYDNEY.

THE Post-Graduate Committee in Medicine announces that a course in clinical pathology will begin on July 29, 1946, for a period of twelve weeks, and will be held at the University of Sydney.

The programme has been arranged to take place in the afternoons from 4.30 to 6.30 o'clock p.m. every Monday, Wednesday and Friday, and will include lecture demonstrations in bacteriology, parasitology, histology, hæmatology and biochemistry. Enrolments are limited to twelve and preference will be given to those candidates who intend taking the diploma examination. An announcement concerning the fees involved will be made shortly and applications should be forwarded to the Secretary of the Post-Graduate Committee, 131, Macquarie Street, Sydney. Telephones: BW 7483, B 4606.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Marrington, John Frederick, M.B., 1945 (Univ. Sydney), 9, Tivoli Street, Mosman.

King, Errol Edward Trevor, M.B., B.S., 1945 (Univ. Sydney), 275, Edgecliff Road, Edgecliff.

Colvin, Cecil Brereton, M.B., B.S., 1942 (Univ. Sydney), Newcastle Street, East Maitland.

Hambly, Colin Keith, M.B., B.S., 1941 (Univ. Sydney), Flat 4, Astor, Pitt Street, Randwick.

Weekes, Hazel Claire, M.B., 1945 (Univ. Sydney), 30, Fairweather Street, Bellevue Hill.

Obituary.

ROBERT WARREN CROOKE.

WE regret to announce the death of Dr. Robert Warren Crooke, which occurred on June 12, 1946, at Wentworthville, New South Wales.

ERNEST JOHN FRAYNE.

WE regret to announce the death of Dr. Ernest John Frayne, which occurred on June 5, 1946, at Adelaide.

Australian Medical Board Proceedings.

TASMANIA.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Act*, 1918, of Tasmania, as duly qualified medical practitioners:

Statham, Cecily Faith, M.B., B.S., 1946 (Univ. Melbourne), General Hospital, Launceston.

Young, Lloyd Alan Forbes, M.B., B.S., 1946 (Univ. Melbourne), General Hospital, Launceston.

Elder, Janet Lucile, M.B., B.S., 1946 (Univ. Melbourne), General Hospital, Launceston.

Long, Winifred Mary, M.B., B.S., 1946 (Univ. Melbourne), General Hospital, Launceston.

Connard, Allan Barrie, M.B., B.S., 1946 (Univ. Melbourne), General Hospital, Launceston.
Lowen, Walter, M.B., B.S., 1945 (Univ. Melbourne), General Hospital, Launceston.
Moloney, William Rex, M.B., B.S., 1939 (Univ. Melbourne), Cameron Street, Launceston.
Suerth, Egon, M.D., 1934 (Messina), Beaconsfield, Tasmania.
Rayment, Dulcie Grace, M.B., B.S., 1943 (Univ. Melbourne), Macquarie Street, Hobart.
Anderson, Arthur Brayton, M.B., Ch.B., 1927 (Univ. Liverpool), Repatriation Department, Hobart.

Notice.

MEMBERS of the New South Wales Branch who have returned to, or commenced practice, and whose telephone numbers do not appear in the recent issue of the telephone directory, may have their number inserted in the "Monthly Notice to Members" upon making a request in writing to the Medical Secretary of the New South Wales Branch.

Books Received.

"The 1945 Year Book of Urology", by Oswald S. Lowsley, M.D., F.A.C.S.; 1946. Chicago: The Year Book Publishers, Incorporated. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 7" x 4¾", pp. 416, with illustrations. Price: 24s.

"The 1945 Year Book of Physical Medicine", edited by Richard Kovács, M.D.; 1946. Chicago: The Year Book Publishers, Incorporated. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 7" x 4¾", pp. 400, with many illustrations. Price: 24s.

"The 1945 Year Book of Industrial and Orthopædic Surgery", edited by Charles F. Painter, M.D.; 1946. Chicago: The Year Book Publishers, Incorporated. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 7" x 4¾", pp. 432, with many illustrations. Price 24s.

"The 1945 Year Book of General Therapeutics", edited by Oscar W. Bethea, Ph.M., M.D., F.A.C.P.; 1946. Chicago: The Year Book Publishers Incorporated. 7" x 4¾", pp. 456, with illustrations. Price: 24s.

"The 1945 Year Book of Neurology, Psychiatry and Endocrinology"; Neurology—edited by Hans H. Reese, M.D., and Mabel G. Masten, M.D.; Psychiatry—edited by Nolan D. C. Lewis, M.D.; Endocrinology—edited by Elmer L. Sevringhaus, M.D.; 1946. Chicago: The Year Book Publishers Incorporated. 7" x 4¾", pp. 720, with illustrations. Price: 24s.

"Ambulatory Proctology", by Alfred J. Cantor, M.D., with a foreword by Beaumont S. Cornell, M.D.; 1946. New York and London: Paul B. Hoeber Incorporated. 9¼" x 6", pp. 544, with many illustrations. Price: $8.00.

"Shock Treatments and Other Somatic Procedures in Psychiatry", by Lothar B. Kalinowsky, M.D., and Paul H. Hoch, M.D., with a foreword by Nolan D. C. Lewis, M.D.; 1946. New York: Grune and Stratton Inc. 8¼" x 5¼", pp. 308. Price: $4.50.

"Doctors, Drugs and Steel", by Edward Podolsky, M.D.; 1946. New York: The Beechhurst Press. Sydney: Angus and Robertson Limited. 9" x 5¾", pp. 384, with illustrations. Price: 26s. 3d.

"Handbook of Infectious Diseases, with Notes on Prophylaxis, Serum Treatment and Vaccination", by the Staff of the Cantacuzène Institute under the direction of Professor C. Ionescu-Mihaesti and Professor M. Ciuca; 1945. Geneva: League of Nations. Sydney: H. A. Goddard Proprietary Limited. 6" x 4¼", pp. 331. Price: 6s. 3d.

Medical Appointments.

Dr. K. H. Grieve has been appointed Assistant Director, Pathological Laboratories, and Medical Officer, Department of Public Health, New South Wales.

Dr. J. H. Crawford, junior, has been appointed Government Medical Officer at Pomona, Queensland.

Dr. Philip Stretton has been appointed certifying medical officer for the Municipality of Queenstown, Tasmania, under the provisions of the *Workers' (Occupational Diseases) Relief Fund Act*.

Dr. Lindsay Dey has been appointed President of the Royal Alexandra Hospital for Children, Camperdown, New South Wales.

Dr. Philip Nolan has been appointed Medical Officer of Health to the Brighton Municipality, Tasmania.

Dr. John Fulton, of Launceston, Tasmania, has been appointed Certifying Medical Officer for the purposes of making the medical examination of nurses under Section 35C of the *Workers' (Occupational Diseases) Relief Fund Act*, 1939.

Diary for the Month.

JUNE 25.—New South Wales Branch, B.M.A.: Ethics Committee.
JUNE 26.—Victorian Branch, B.M.A.: Council Meeting.
JUNE 27.—South Australian Branch, B.M.A.: Scientific Meeting.
JUNE 27.—South Australian Branch, B.M.A.: Council Meeting.
JUNE 27.—New South Wales Branch, B.M.A.: Branch Meeting.
JUNE 28.—Queensland Branch, B.M.A.: Council Meeting.
JULY 2.—New South Wales Branch, B.M.A.: Council Quarterly.
JULY 3.—Victorian Branch, B.M.A.: Branch.
JULY 3.—Western Australian Branch, B.M.A.: Council Meeting.
JULY 5.—Queensland Branch, B.M.A.: Branch Meeting.
JULY 9.—Tasmanian Branch, B.M.A.: Ordinary Meeting.
JULY 9.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
JULY 9.—New South Wales Branch, B.M.A.: Organization and Science Committee.
JULY 11.—South Australian Branch, B.M.A.: Council Meeting.
JULY 12.—Queensland Branch, B.M.A.: Council Meeting.
JULY 16.—New South Wales Branch, B.M.A.: Medical Politics Committee.
JULY 17.—Western Australian Branch, B.M.A.: General Meeting.
JULY 18.—New South Wales Branch, B.M.A.: Clinical Meeting.
JULY 18.—Victorian Branch, B.M.A.: Executive Meeting.
JULY 23.—New South Wales Branch, B.M.A.: Ethics Committee.
JULY 24.—Victorian Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

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